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SAFER PRESCRIBING OF SEDATIVE-HYPNOTICS GUIDELINE

SCOPE: This Safer Prescribing of Sedative-hypnotic Medication Guideline is intended to offer prescribing guidance for providers, clients and the interested general public to increase the effectiveness and safety of sedative-hypnotic use. It is not intended to be comprehensive in scope. These recommendations are not a substitute for clinical judgment. Decisions about care must carefully consider and incorporate the clinical characteristics and circumstances of each individual. If you have further questions about sedative-hypnotics, contact the CBHS Drug Information Consultation Service (druginfo.bhs@sfdph.org).

INTRODUCTION: Sedative-hypnotics are prescribed for multiple conditions in mental health, most often for acute anxiety and insomnia. See introduction and treatment guidelines in the references and further reading section at the end of this document for suggested treatment algorithms for the use of these medications.

Unlike most other medications commonly prescribed in mental health settings, sedative-hypnotics have a high incidence of misuse, abuse and diversion. These medications are associated with memory impairment, can affect the ability to safely operate motor vehicles, and can increase the risk of falls. They have significant risks for respiratory depression and even death in combination with other CNS depressants including opioids and/or alcohol. Because of these safety concerns BHS recommends using alternatives to sedative-hypnotic medication as first line therapy. If sedative-hypnotic medication is prescribed, then short-term use is preferred (less than two weeks). For more chronic use, there are specific treatment recommendations in the next section.

The selection of a specific sedative-hypnotic medication, form of administration, dose and duration of treatment is a complex decision-making process involving multiple factors. These factors often include individualized treatment goal(s), client choice, history of past medication trials, family history, side effect profile and others.

TREATMENT RECOMMENDATIONS FOR SEDATIVE-HYPNOTIC USE: Sedative-hypnotics are most often prescribed for anxiety and/or insomnia in mental health settings. There are numerous effective and safer non-medication and non-sedative-hypnotic medication therapies for these conditions. All clients should first be offered these treatments. See Appendix 2 for more information on the treatment of insomnia and Appendix 3 for information on the treatment of anxiety, trauma and obsessive-compulsive disorders. Appendix 4 contains information about herbal supplements.

All clients being considered for a sedative-hypnotic medication should have a complete evaluation, including a CURES report (California's prescription drug monitoring program) to identify any prescribed scheduled substances. Note that CURES does not include methadone from methadone treatment facilities. Specific risk factors that could lead to poor outcomes should be identified and documented. Risk factors include:

- Current or previous alcohol or substance use disorder
- History of overdose
- Fall risk
- Traumatic brain injury
- Memory problems
- Sleep apnea
- Age >60
- Chronic obstructive pulmonary disease

CURES reports and risk factors should be reviewed every 6 months during treatment with sedative-hypnotics. Clients with significant risk factors should be offered alternative non-sedative-hypnotic therapies. If clients with significant risk factors are currently taking sedative-hypnotics, they should be tapered off them unless there is a documented justification for continuing treatment.

When starting sedative-hypnotics, initial prescriptions should be limited in quantity and dose. Clients should be informed that these medications are high risk for adverse events in chronic use. If use greater than two weeks is indicated, providers should document a justification. Providers should consistently document attempts to change to non-medication or non-sedative-hypnotic medication therapies.

Special attention should be paid to clients receiving opioid medication therapy as well as sedative-hypnotic therapy. In combination, there is a significantly increased risk of respiratory depression, over-sedation, and accidental overdose death. Providers should clearly document the justification for such combination therapy and an evaluation of risk. Prescribers should consult with their colleagues about these cases. Clients should be offered naloxone rescue kits with instructions and training on their use. Providers should coordinate care with the opioid prescriber. If clients decline to provide consent for care coordination with their opioid prescriber, the prescribing of sedative-hypnotics is not recommended.

BENZODIAZEPINES

Introduction: Benzodiazepines are used for various indications including anxiety, panic disorder, alcohol withdrawal, seizures, catatonia, mania, agitation, muscle spasms, and insomnia. This guideline refers to the use of benzodiazepines for anxiety, panic disorder, and insomnia. The use of benzodiazepines for other indications is beyond the scope of this guideline. Please refer to SFHN BHS Medication Approaches to Alcohol Use Disorder Guideline for details on how to use benzodiazepines in the management of alcohol withdrawal. Please refer to the SFHN

BHS Safer Use of Mood Stabilizers Guideline for information on the use of benzodiazepines for agitation in acute mania.

Benzodiazepines work by binding to the γ subunit of the GABA-A receptor, thereby causing an allosteric modification of the receptor which increases the receptor activity. By doing so, benzodiazepines increase the frequency of channel opening events, increasing chloride ion conductance and inhibiting the action potential.

Due to the delayed onset of therapeutic action for antidepressant medications, benzodiazepines are used for rapid, symptomatic treatment of anxiety and panic disorder. They are also used for insomnia due to their sedating effect. Benzodiazepines differ in their onset of action, duration of action and relative potency. See Table 1 below for details on specific benzodiazepines.

TABLE 1: BENZODIAZEPINE DOSAGE FORMS AND PHARMACOKINETICS

Generic name	**Dosage forms**	**Onset of Action[1]**	**Relative Potency (mg) [2]**	**Duration (hours)[2]**
Alprazolam	IR Tab: 0.25, 0.5, 1, 2mg Oral solution: 1mg/mL ODT tab: 0.25, 0.5, 1, 2mg XR tab: 0.5, 1, 2, 3mg	Intermediate	0.5	IR: 5 XR: 11
Chlordiazepoxide	Cap: 5, 10, 25mg	Intermediate	10	
Clonazepam	Tab: 0.5, 1, 2mg ODT tab: 0.125, 0.25, 0.5, 1, 2mg	Intermediate	0.25-0.5	12
Diazepam	Tab: 2, 5, 10mg Oral solution: 5mg/mL Injection: 5mg/mL Rectal gel: 5mg/mL	Rapid	5	Variable (dose and frequency dependent)
Flurazepam	Capsule: 15, 30mg	Rapid	15	7-8
Lorazepam	Tab: 0.5, 1, 2mg Oral solution: 2mg/mL Injection: 2mg/mL, 4mg/mL	Intermediate (PO tab) Rapid (Soln, Inj)	1	6-8
Midazolam	Oral syrup: 2mg/mL Injection: 1mg/mL, 5mg/mL	Rapid	5 (PO) 2 (IV)	2
Oxazepam	Cap: 10, 15, 30mg	Slow	15-30	
Temazepam	Cap: 7.5, 15, 22.5, 30mg	Slow	10	
Triazolam	Tab: 0.125, 0.25mg	Intermediate	0.25	6-7

1. Rapid onset= within 15 minutes, Intermediate= 15-30 minutes, Slow= 30-60 minutes
2. Approximate. Duration of action is determined by redistribution rather than by metabolism, therefore half-life is not a good determination of duration of action (LexiComp Drug Information Handbook).

Benzodiazepines with faster onsets of action and shorter half-lives tend to have higher abuse potential and increased risk and severity of withdrawal syndromes. Common adverse effects of benzodiazepines include confusion, dizziness, sedation, short-term memory loss, disinhibition, ataxia, blurred vision, slurred speech, and muscle weakness. Benzodiazepines are associated with

an increased risk of hip fractures when used short-term in older adults. Benzodiazepines can impair the ability to drive a vehicle or operate heavy machinery.

Long-term use of benzodiazepines is associated with depression, cognitive impairment, increased rates of motor vehicle crashes, increased rates of falls and hip fractures, and increased rates of mortality. Chronic exposure to benzodiazepines alters the regulation of GABA-A receptor subunits and can lead to tolerance, physical dependence, and withdrawal. Investigations of the association between use of benzodiazepines and cognitive decline have yielded mixed results. However, there is a body of evidence suggesting chronic benzodiazepine use is associated with cognitive decline and dementia. Chronic use of benzodiazepines is not recommended.

Benzodiazepines are not recommended for use in Post-Traumatic Stress Disorder as they are associated with lack of efficacy, worse overall severity, worse psychotherapy outcomes, aggression, depression, and substance use. They may interfere with the extinction of fear conditioning and/or potentiate the acquisition of fear responses and worsen recovery from trauma.

Drug Interactions: See Appendix 1 (Table 5) for information about drug interactions.

Discontinuation after Chronic Use: Discontinuing benzodiazepines after chronic daily administration is associated with withdrawal symptoms including sleep disturbances, irritability, panic attacks, hand tremor, sweating, difficulty concentrating, nausea, dry retching, headaches, palpitations, muscular pain/stiffness, and perceptual changes. Very serious withdrawal may include seizures or psychotic reactions. Withdrawal phenomena tend to be more severe following withdrawal from high doses or short-acting benzodiazepines. Benzodiazepines should always be tapered rather than ceased abruptly, unless a very severe adverse effect requires rapid discontinuation.

The EMPOWER trial mailed 148 chronic benzodiazepine consumers aged 65-95 an 8-page education brochure on the risks of taking sedative-hypnotics along with a picture of a 20-week tapering protocol. After 6 months, 27% of individuals who received this intervention had discontinued their benzodiazepines and an additional 11% had reduced their dose. This handout can be given to clients as an educational tool to support clients during a taper of a sedative-hypnotic: https://www.sfdph.org/dph/files/CBHSdocs/EmpowerPatientHandout.pdf

Pregnancy: The following benzodiazepines have documented positive evidence of teratogenic risk: alprazolam, chlordiazepoxide, clonazepam, diazepam, lorazepam and oxazepam. Flurazepam, temazepam, triazolam are contraindicated in pregnancy. The use of benzodiazepines during the first trimester may be associated with a slightly increased risk for oral cleft; however, the overall risk remains less than 1%. Maternal use of benzodiazepines in the third trimester is associated with floppy infant syndrome which consists of hypothermia, lethargy, poor respiratory effort, and feeding difficulties. Maternal use in the third trimester is also associated with infant withdrawal syndromes that may persist for several months after delivery.

Lactation: The American College of Obstetrics and Gynecology (ACOG) rates benzodiazepines as L3, moderately safe, and generally views benzodiazepines as compatible with breastfeeding.

Shorter acting benzodiazepines are preferred in order to minimize any effect on the breastfed infant. Benzodiazepines are generally found in low levels in breastmilk. Reports of sedation, poor feeding, and respiratory distress have been published and are mostly associated with longer acting benzodiazepines such as diazepam and clonazepam. Pre-term infants and newborns may have reduced ability to metabolize benzodiazepines, and there is concern about medication accumulation in those infants. Adverse effects in infants are rare with lorazepam, midazolam, and oxazepam, so these are the preferred benzodiazepines in breastfeeding women.

Pediatrics: Benzodiazepines have not been well studied in children and adolescents. Due to the associated adverse effects, risk of dependence, and the possibility of a "paradoxical response", their use should be limited in this population. Long-term use is not recommended. There is not good clinical trial data supporting the long-term use of benzodiazepines for insomnia or other disorders. Pharmacologic treatment of insomnia in pediatric patients varies widely with little data to support long term use of these agents. Other agents such as antihistamines and alpha-adrenergic receptor agonists have been used in pediatric populations to target both insomnia and anxiety; however, the clinical trial data is lacking for the long-term use of these agents in pediatric populations as well.

Older Adults: Older adults are more sensitive to potential side effects of benzodiazepines due to altered pharmacokinetics and pharmacodynamics. Some benzodiazepines undergo Phase I metabolism, which include hepatic oxidation and reduction reactions, while others undergo Phase II metabolism, which include glucuronidation reactions. Phase I metabolism is reduced in older adults while Phase II remains relatively preserved. Benzodiazepines with oxidative pathways and longer half-lives, such as diazepam and flurazepam, are more likely to accumulate in the body and cause prolonged effects. Lorazepam, oxazepam, and temazepam undergo Phase II glucuronidation and are preferred over other benzodiazepines in older adults. Adverse effects in older adults, including sedation, ataxia, falls, delirium, short and long-term cognitive impairment, and disinhibition contribute to increased mortality and higher rates of hospitalization. The risk of dependence in older adults increases with age and is more likely among those with multiple medical conditions, depression, and alcohol use disorder.

The American Geriatrics Society (AGS) publishes a list of potentially inappropriate medications for older adults. The current AGS recommendation is to avoid all benzodiazepines in most adults age 65 years of age or older. When the use of these agents is unavoidable they should be initiated at lower doses, monitored carefully, and used short-term only. Consider reducing the use of other CNS active medications that increase the risk of falls if the patient has a history of falls and a safer agent is not available.

Renal and Hepatic Impairment: See Appendix 1 (Table 4) for information on the use of benzodiazepines in individuals with renal and hepatic impairment. Practice caution if using benzodiazepines in renal or hepatic impairment.

NON-BENZODIAZEPINE RECEPTOR AGONISTS [NBRAs, "z-drugs"]

Introduction: NBRAs (often referred to as z-drugs) include zolpidem, zaleplon, and eszopiclone. While they are not chemically related to benzodiazepines based on their molecular structures, they bind to central benzodiazepine receptors as agonists. They are approved for use in treating sleep-onset insomnia due to their capacity to decrease sleep latency. Eszopiclone and extended-release zolpidem may be used for sleep maintenance.

Considerations when Initiating Treatment: Table 2 below lists recommended dosage ranges for NBRAs. Current labeling for zolpidem recommends that lower doses be used in women because of reported greater increases in serum concentrations compared with men that could impair the ability to drive or other activities that require mental alertness. Prolonged elevated levels into the following day may also be seen after taking extended-release zolpidem. The FDA also recommends that the starting dose of eszopiclone for all individuals be reduced to 1 mg because of reports of impaired driving skills, memory, and coordination for almost 12 hours after taking an evening dose.

TABLE 2: NBRA DOSAGES AND PHARMACOKINETICS

Generic name	Dosage forms	Onset of Action	Duration	Usual Dose (mg)
Eszopiclone	Tablet: 1, 2, 3 mg	<30 minutes	~8 hours	1-3
Zaleplon	Capsule: 5, 10 mg	<30 minutes	~4 hours	10-20
Zolpidem (immediate-release)	Tablet: 5, 10 mg	<30 minutes	~8 hours	Men: 5-10 Women: 5
Zolpidem (extended-release)	ER tablet: 6.25, 12.5 mg	<30 minutes	~8 hours	Men: 6.25-12.5 Women: 6.25
Zolpidem (sublingual)	Tablet (*Edular*): 5, 10 mg	<30 minutes	~8 hours	Men: 5-10 Women: 5
	Tablet (*Intermezzo*): 1.75, 3.5 mg	20 minutes	~4 hours	Men: 3.5 Women: 1.75
Zolpidem (oral spray)	Spray: 5 mg/100 µL spray	20 minutes	~8 hours	Men: 5-10 Women: 5

Adverse Effects: Common adverse effects of NBRAs include drowsiness, dizziness, and headache. NBRAs can potentially impair next-day cognitive performance and driving ability. Other complex sleep-related behaviors that have been reported with NBRAs include sleep-walking, sleep-eating, and sleep-driving; emergence of these adverse events warrant discontinuation of the medication. NBRA's are associated with an increased risk of hip fractures when used short-term. NBRAs are controlled substances (Schedule IV) that carry risks of withdrawal, dependence, and abuse.

Drug Interactions: See Appendix 1 (Table 5) for information about NBRA drug interactions.

Pregnancy: There are no adequate, well controlled studies of NBRAs in pregnant women. The risks of teratogenicity associated with NBRAs cannot be ruled out.

Lactation: Zolpidem and zaleplon are known to be excreted in human milk; similar information is not known for eszopiclone. Caution should be exercised when administering NBRAs to a nursing woman.

Pediatrics: The safety and effectiveness of NBRAs have not been established in pediatric patients, so their use cannot be recommended. Controlled clinical studies of their use in pediatric patients with insomnia due to Attention-Deficit Hyperactivity Disorder failed to demonstrate efficacy and there were some reports of hallucinations in children during the studies.

Older Adults: Lower doses of NBRAs in older adults are recommended to minimize adverse events associated with impaired motor and/or cognitive performance, potential for falls, and unusual sensitivity to sedative-hypnotic medications.

Renal and Hepatic Impairment: See Appendix 1 (Table 4) for information on the use of NBRAs in individuals with renal and hepatic impairment.

OREXIN ANTAGONISTS

Introduction: Orexin antagonists are the newest class of sedative-hypnotics; they include lemborexant, suvorexant, and daridorexant. Their mechanism of action involves blocking the orexin receptors OX_{1R} and OX_{2R}. The orexin signaling system is a central promoter of wakefulness; by blocking this signal orexin antagonists are thought to suppress the wake drive. They are indicated for the treatment of insomnia, characterized by difficulties with sleep onset and/or sleep maintenance. They are contraindicated in individuals with narcolepsy. See Table 3 for dosing information.

TABLE 3: OREXIN ANTAGONISTS DOSING AND PHARMACOKINETICS

Generic name	Dose range	Time to peak	Duration (hours)	Comments
Lemborexant	5-10mg	1-3 hours	7+	Time to effect delayed by ~2 hours if taken with a meal
Suvorexant	5-20mg	2 hours	7+	Time to effect delayed by ~1.5 hours if taken with a meal
Daridorexant	25-50 mg	1-2 hours	8+	Time to effect delayed by ~1.3 hours if taken with a meal

Adverse Effects/Warnings: The most common side effects of orexin antagonists include somnolence, headache, and abnormal dreams. Women and obese individuals tend to have higher blood levels of suvorexant compared to men and non-obese individuals at similar doses. This was not observed with the use of lemborexant or daridorexant. Prescribers should carefully

assess for dose-related side effects prior to increasing the dose of suvorexant in women and obese individuals.

There are several warnings associated with the use of orexin antagonists. As they are central nervous system (CNS) depressants, individuals should be monitored for daytime somnolence. They can impair driving and increase the risk of falling asleep while driving. Individuals should be monitored for worsening of depression or suicidal ideation while on these medications. Prescribing the lowest feasible number of tablets is advisable in individuals at risk for suicidal behavior. Complex behaviors such as sleep-driving, sleep-eating, amnesia, and hallucinations have been reported with these medications. If any of these behaviors occur, orexin antagonists should be discontinued. Sleep paralysis and hypnagogic/hypnopompic hallucinations may occur. Prescribers should counsel individuals about the possibility and nature of these events.

Drug Interactions: The major metabolic pathway for orexin antagonists is via CYP3A4. See Appendix 1 (Table 5) for information about drug interactions.

Pregnancy: No human data has been published regarding teratogenic risk. Consider enrolling in pregnancy registry if using medication during pregnancy.

Lactation: It is not known whether orexin antagonists are secreted in human milk; caution should be exercised if medications are administered to a nursing individual.

Pediatrics: Suvorexant, lemborexant, and daridorexant have not been studied in pediatric patients and their use is not recommended.

Older Adults: No meaningful differences in safety or effectiveness were seen for older adults treated with suvorexant in clinical trials. No dose adjustments are recommended at this time. Adults >65 years experienced more somnolence on the 10mg dose of lemborexant compared to adults <65 years. Caution should be used for doses >5mg in adults >65 years.

Renal and Hepatic Impairment: See Appendix 1 (Table 4) for information on the use of orexin antagonists in individuals with renal and hepatic impairment.

APPENDIX 1: SEDATIVE-HYPNOTIC DOSING REFERENCE TABLES

TABLE 4: SEDATIVE-HYPNOTIC USE IN RENAL AND HEPATIC IMPAIRMENT

Generic Name	Renal Impairment	Hepatic Impairment
BENZODIAZEPINES		
Alprazolam	No dose adjustments	No dose adjustments
Chlordiazepoxide	CrCl $\geq$ 10ml/min: No dose adjustment CrCl$\leq$ 10ml/min: Reduce dose by 50% Dialysis: Reduce dose by 50%	Undergoes hepatic metabolism. No dose adjustment recommendation provided
Clonazepam	Metabolites may accumulate No dose adjustment recommendation provided	Undergoes hepatic metabolism Contraindicated in significant hepatic impairment.
Diazepam	No dose adjustments	Mild-to-moderate: Reduce dose by 50% Severe: use is contraindicated
Flurazepam	No dose adjustments	No dose adjustments
Lorazepam	No dose adjustments Use is not recommended in severe renal impairment.	No dose adjustments for mild-to-moderate impairment Lower doses may be required for severe impairment.
Midazolam	No dose adjustments Half-life of drug and metabolites may be prolonged.	Duration of action may be prolonged Consider reducing dose if using multiple doses.
Oxazepam	No dose adjustments	No dose adjustments Hepatic dysfunction not expected to decrease drug clearance
Temazepam	No dose adjustments	No dose adjustments
Triazolam	No dose adjustments	No dose adjustments
NBRAs (“Z-DRUGS”)		
Eszopiclone	No dose adjustments in mild to moderate impairment (not studied in severe impairment)	No dose adjustments
Zaleplon	No dose adjustments in mild to moderate impairment (not studied in severe impairment)	Dose reduced in mild to moderate impairment
Zolpidem	No dose adjustments in mild to moderate impairment (not studied in severe impairment)	Dose reduced in mild to moderate impairment
OREXIN ANTAGONISTS		
Daridorexant	No dose adjustments	No dose adjustments for mild to moderate impairment (not

		recommended for severe impairment)
Lemborexant	No dose adjustments	No dose adjustments for mild to moderate impairment (not recommended for severe impairment)
Suvorexant	No dose adjustments	No dose adjustments for mild to moderate impairment (not recommended for severe impairment)

TABLE 5: SEDATIVE-HYPNOTIC DRUG INTERACTIONS

Interaction	Clinical Concern/Comments/Recommendation
BENZODIAZEPINES	
CNS depressants (e.g., opioids, alcohol)	Increased risk of overdose and death. Avoid concomitant use.
CYP3A4 inducers (e.g., carbamazepine, phenytoin)	Decreases levels of alprazolam, clonazepam and diazepam which are metabolized by CYP3A4.
CYP3A4 inhibitors (e.g., fluconazole, diltiazem, grapefruit juice)	Increases levels of alprazolam, clonazepam and diazepam which are metabolized by CYP3A4.
Omeprazole	Increases the concentration of diazepam and prolongs its half-life.
Estrogen containing contraceptives	Increases the concentration of alprazolam. Decreases the concentration of lorazepam, oxazepam and temazepam which are metabolized via glucuronidation.
NBRAs (“Z-DRUGS”)	
Alcohol, opioids, other CNS depressants	Additive CNS depressant effects. Avoid combination to reduce risk
CYP3A4 inhibitors (e.g., ketoconazole, clarithromycin)	Decreases in NBRA metabolism may lead to their accumulation with increased risk of toxicity. Use of lower doses may be warranted
CYP3A4 inducers (e.g., rifampin)	Increases in NBRA metabolism may lead to decreased levels and reduced effectiveness. Use of higher doses may be warranted
OREXIN ANTAGONISTS	
CNS depressants (e.g., opioids, alcohol)	Additive CNS depressant effects. Avoid concomitant use due to increased risk of CNS depression
Weak CYP3A4 inhibitors (e.g., ranitidine, cimetidine)	Decreases in orexin antagonist metabolism may lead to their accumulation with increased risk of toxicity Lemborexant: Maximum dose is 5mg Suvorexant: No adjustment needed
Moderate CYP3A4 inhibitors (e.g., atazanavir, ciprofloxacin,	Decreases in orexin antagonist metabolism may lead to their accumulation with increased risk of toxicity Lemborexant: Avoid concomitant use

fluconazole, diltiazem, grapefruit juice)	Suvorexant: Decrease dose to 5mg Daridorexant: Maximum dose is 25mg
Strong CYP3A4 inhibitors (e.g., ketoconazole, ritonavir, nefazodone)	Decreases in orexin antagonist metabolism may lead to their accumulation with increased risk of toxicity. Avoid concomitant use with orexin antagonists
Strong and moderate CYP3A4 inducers (e.g., phenytoin, carbamazepine, rifampin, modafinil, St. John's wort)	Increases in orexin antagonist metabolism may lead to decreased levels and reduced effectiveness. Lemborexant: Avoid concomitant use Suvorexant: Efficacy may be reduced

APPENDIX 2: NON-SEDATIVE-HYPNOTIC TREATMENT OF INSOMNIA

Insomnia is often a symptom of a comorbid condition. Left untreated over time, patients may develop numerous psychological and behavioral issues that exacerbate insomnia, worrying about inability to sleep or daytime consequences of poor sleep, having distorted beliefs about the origin or meaning of insomnia, making schedule changes to accommodate the insomnia, and spending excessive time in bed. Treatment of insomnia should begin by treating comorbidities (such as major depression, pain, and movement disorders) or by eliminating activating medications. Psychologic and behavioral treatment should restructure maladaptive cognitions and establish healthy sleep habits/environments. Short term pharmacological treatment may be used to supplement these therapies. See References section for more information.

PATIENT RESOURCES:

SLEEP DIARY: This can be used by patients to track their sleep patterns.
https://www.sfdph.org/dph/files/CBHSdocs/SleepDiary.pdf

SLEEP HABITS DO'S AND DON'TS**:** The American Academy of Sleep Medicine recommends that patients practice good sleep hygiene techniques in combination with other treatments for insomnia. This is an easy-to-read handout that reviews healthy sleep habits that can be given directly to patients.
English: https://www.sfdph.org/dph/files/CBHSdocs/SleepHabits-ENGLISH.pdf
Spanish: https://www.sfdph.org/dph/files/CBHSdocs/SleepHabits-SPANISH.pdf
Chinese: https://www.sfdph.org/dph/files/CBHSdocs/SleepHabits-CHINESE.pdf
Vietnamese: https://www.sfdph.org/dph/files/CBHSdocs/SleepHabits-VIETNAMESE.pdf
Tagalog: https://www.sfdph.org/dph/files/CBHSdocs/SleepHabits-TAGALOG.pdf
Russian: https://www.sfdph.org/dph/files/CBHSdocs/SleepHabits-RUSSIAN.pdf

PROVIDER RESOURCES:

CBT: CBT geared specifically for insomnia (CBT-I) has been found to improve sleep quality, reduce use of sedative-hypnotic medications and improve quality of life in a cost-effective manner. These handouts are outlines of CBT-I sessions and can be used by providers as a guide for nonpharmacological management of insomnia:
https://www.sfdph.org/dph/files/CBHSdocs/CBTforInsomniaHandout.pdf

SLEEP CLINIC REFERRAL: Sleep studies can be beneficial for ruling out medical causes of insomnia such as sleep apnea.

UCSF Sleep Disorders Center | UCSF Health
(415) 885-7886
Refer by medical provider: Any physician, regardless of specialty, can refer patients
Download referral form and FAX from this link:
https://www.ucsfhealth.org/clinics/sleep-disorders-center
Insurance accepted:
- Medi-Cal (San Francisco residents only)
- Medicare (referred by UCSF, SF hospital, or SF clinic)
- San Francisco Health Network: Need pre-authorization (usually submitted by primary care) required for specialty or hospital care

Urgent consults: Take 72 hours

Non-urgent consults: Take more than 72 hours depending on the volume of patients; will be performed as soon as possible
Visit with sleep specialist required after receipt of referral (sleep specialist will decide need for inpatient overnight study or outpatient monitoring)

NON-SEDATIVE-HYPNOTIC MEDICATIONS:
Non-sedative-hypnotic medications are preferred to sedative-hypnotic medications as the first line pharmacological treatment of insomnia. Table 6 below provides recommendations for non sedative-hypnotic medication therapy for insomnia.

TABLE 6: NON-SEDATIVE-HYPNOTIC MEDICATIONS FOR INSOMNIA:

Name	Dosage Range	Mechanism	Comments
Doxepin*	3-10mg	Tricyclic antidepressant	Doses >10mg will have anticholinergic effects
Gabapentin	100-1200mg	Structurally related to GABA, may modulate the release of excitatory neurotransmitters	May also be helpful for neuropathic pain
Mirtazapine*	7.5-45mg	Central presynaptic alpha-2 antagonist	Lower doses are more sedating; may increase appetite and triglycerides; may cause weight gain
Ramelteon	8mg	Melatonin receptor agonist	Mild therapeutic effect, not covered by many insurance companies
Trazodone*	12.5-300mg	Potentiates serotonergic activity in the CNS	Start at low doses, may cause "hangover" feeling in the morning

*See related SFHN BHS Safer Prescribing of Antidepressant Medications Guideline for more information on these medications

APPENDIX 3: NON-SEDATIVE-HYPNOTIC TREATMENT OF ANXIETY, TRAUMA AND OBSESSIVE-COMPULSIVE DISORDERS

GENERAL CONSIDERATIONS: Anxiety, trauma, and obsessive-compulsive disorders encompass a group of conditions including but not limited to Generalized Anxiety Disorder (GAD), Panic Disorder (PD), Social Anxiety Disorder (SAD), Post-Traumatic Stress Disorder (PTSD), and Obsessive-Compulsive Disorder (OCD). These disorders may present alone or co-occur with other psychiatric conditions such as Depression, Bipolar Disorder, Schizophrenia, and Substance Use Disorders.

Proper diagnosis and treatment of other psychiatric conditions may alleviate anxiety, such as antipsychotics for schizophrenia or mood stabilizers for mania. Anxiety may manifest as a symptom of an underlying medical problem or as a side-effect of medications.

Treatment of these disorders should begin by evaluating for and treating any underlying medical problems and by targeting any contributory medications. These disorders may be treated with non-pharmacological interventions, such as psychotherapy and behavioral treatments, as well as with medications. Selective serotonin reuptake inhibitors (SSRIs) are recommended as first line pharmacologic treatment for anxiety, trauma and obsessive-compulsive disorders.

PSYCHOTHERAPY AND BEHAVIORAL TREATMENT: Psychotherapy can help uncover underlying causes of fears, teach clients how to relax and decrease anxiety responses, look at situations in new ways and develop better coping and problem-solving skills. Many people find relief from acute symptoms in 8-10 weeks of focused therapy, with ongoing treatment helpful in maintaining and supporting change. In general, the types of psychotherapy most studied and found to be effective focus on cognitive and behavioral change. Some psychotherapeutic techniques include:

- Cognitive Behavioral Therapy (CBT)
- Behavioral Techniques
- Acceptance and Commitment Therapy (ACT)
- Prolonged Exposure Therapy (PE)
- Cognitive Processing Therapy (CPT)
- Relaxation Techniques
- Breathing Exercises
- Stress Reduction
- Lifestyle changes including diet and physical exercise

There are many self-help manuals available with detailed instructions and worksheets. Example worksheets are available on the CBHS website. Mobile applications can be effective tools that make therapy more accessible, efficient, and portable for those suffering with anxiety. The Anxiety and Depression Association of America has reviewed several apps for anxiety. Clients and providers can find more information about those apps at www.adaa.org.

MOBILE PHONE APPLICATIONS:

These apps are not intended to be used as self-help without the guidance of a professional mental health care provider.

Acceptance and Commitment Therapy (ACT) Coach

- The App provides patients with exercises, tools, information and tracking logs to help them practice what they learn in therapy in their daily life.
- ACT can be useful for anyone who struggles with depression, anxiety, posttraumatic stress disorder or other trauma-related difficulties.

Features include:

- Six mindfulness exercises to practice the ACT core concepts of acceptance and willingness
- Tools to help identify personal values and to take concrete actions to live by them
- Logs for keeping track of useful coping strategies and willingness to practice ACT skills

Prolonged Exposure (PE) Coach

- PE Coach provides tools for patients using PE Therapy to reduce their symptoms of PTSD.
- PE Coach is integrated with smartphone calendar functionality to encourage patient recall and session attendance.
- The App can be useful to any trauma survivor participating in PE treatment.

Features Include:

- Audio and visual information about PE and common reactions to trauma.
- Capability for audio recording of PE therapy sessions directly onto the patient's mobile device.
- PTSD symptom tracking over time to evaluate treatment progress and outcomes.
- Tools to support patient tasks between sessions.
- An interactive breathing retraining coach.

Cognitive Processing Therapy (CPT) Coach

- The App contains support materials for a complete course of CPT to help patients manage their treatment, including between session assignments, readings, PTSD symptom monitoring and mobile versions of CPT worksheets.
- CPT has been shown to be one of the most effective treatments for PTSD from both civilian and military-related traumas.

Features Include:

- An assessment tool for tracking symptoms and progress
- CPT homework assignments and worksheets for each session
- Reminders for therapy sessions
- Educational materials about CPT and its treatment components

CPT Coach is not a self-help tool for patients. It is designed to be used interactively by both clinician and patient as an aide to face-to-face treatment using CPT principles. A requirement for successful use of this App by health care providers is formal clinical training in CPT. This app does not provide training in CPT and will not serve as a substitute for this training.

MEDICATIONS: Selective Serotonin Reuptake Inhibitors are the medication class with the most evidence to support their use in anxiety, trauma and obsessive-compulsive disorders. See Table 7 below for information on other medications with some evidence for their use in the various disorders. Tables 8 and 9 provide more details about the use of these medications.

TABLE 7: MEDICATION GUIDE FOR ANXIETY, TRAUMA, AND OBSESSIVE-COMPULSIVE DISORDERS

	Generalized Anxiety Disorder	Panic Disorder	Social Anxiety Disorder	Post-Traumatic Stress Disorder	Obsessive-Compulsive Disorder
***Selective Serotonin Reuptake Inhibitors**	√	√	√	√	√
***Serotonin Norepinephrine Reuptake Inhibitors**	√	√	√	√	√
***Mirtazapine**	√	√	√	√	
***Tricyclic Antidepressants**	√	√		√	√
***Monoamine Oxidase Inhibitors**		√	√	√	
Buspirone	√				
Hydroxyzine	√				
Pregabalin	√		√		
Gabapentin	√		√		
Propranolol			√ (performance anxiety)		
Prazosin				√ (nightmares)	
Clonidine/guanfacine				√	
Nefazodone				√	

√ Evidence exists for the use of this medication or medication class for this indication
*See related SFHN BHS Safer prescribing of antidepressant medication guideline for more information on these medications

TABLE 8: DOSING INFORMATION

Medication	Daily Dose Range	Renal Adjustment	Hepatic Adjustment	Comments
Buspirone	10-60mg	No	No	Works best when used in conjunction with SSRIs/SNRIs. Onset of effect is delayed by 2 weeks, so best if doses daily rather than PRN.
Hydroxyzine	25-400mg	Yes	Yes, in cirrhosis	May be helpful for symptomatic use in the short term. Anticholinergic, especially at high doses; refer to SFHN BHS Safer Prescribing of Antipsychotic Medications Guideline for more information about the risks of anticholinergic medications.
Pregabalin	150-600mg	Yes	No	May be helpful for discontinuing long term benzodiazepines for those with GAD. Upon discontinuation, dose should be tapered over a week.
Gabapentin	100-1200mg TID	Yes	No	
Propranolol	10-240mg in divided doses	No	No	**Avoid in patients with asthma or other airway disease**. Monitor blood pressure and heart rate.
Prazosin	1-15mg	Titrate cautiously	No	Helpful for trauma-related nightmares. Start with 1mg and titrate carefully, monitoring blood pressure. Watch out for first dose effect
Clonidine	0.1-0.6mg	Use lower initial doses and monitor closely	No	Decreases sympathetic outflow from the CNS. May be helpful for agitation and hyperarousal not adequately treated by SSRIs. Monitor blood pressure and pulse.
Guanfacine	1-4mg	Use lower doses	Use caution	Decrease sympathetic outflow from the CNS. May be helpful for agitation and hyperarousal not adequately treated by SSRIs. Monitor blood pressure and pulse.
Nefazodone	200-600mg in divided doses	No	Use caution	Take on an empty stomach. **Risk of hepatotoxicity; do not use with known liver disease.** Monitor LFTs every 3-6 months and discontinue therapy if AST/ALT reach 3x or greater the upper limit of normal.

TABLE 9: INFORMATION ABOUT PREGNANCY AND LACTATION

Medication	Pregnancy Considerations	Lactation
Buspirone	Animal studies have failed to demonstrate a risk to the fetus and there are no adequate and well-controlled studies in pregnant women	Not recommended
Hydroxyzine	Contraindicated	Not recommended
Pregabalin	Crosses the placenta; studies evaluating neonatal outcomes following exposure during pregnancy are limited	Not recommended
Gabapentin	Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks	Relatively compatible with breastfeeding; monitor infants for drowsiness, adequate weight gain and developmental milestones
Propranolol	Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks	Compatible with breastfeeding at usual doses; monitor infants for bradycardia, cyanosis and hypoglycemia
Prazosin	Limited use in pregnant women has not demonstrated any fetal abnormalities or adverse effects	Use caution
Clonidine	Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled	Use caution; avoid using when nursing infants born <34 weeks gestation

	studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks	
Guanfacine	Animal studies have failed to demonstrate a risk to the fetus and there are no adequate and well-controlled studies in pregnant women	Use caution
Nefazodone	Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks	Use caution

APPENDIX 4: HERBAL SUPPLEMENTS

In the US, herbal supplements are not regulated by the FDA. Purity and potency of available products are unknown. The regulations surrounding herbal supplements do not guarantee that they are effective or safe for anyone to use. Supplements should be reviewed for possible adverse effects and drug interactions before being cleared for client use. Most insurance plans do not cover herbal supplements, so clients may have to pay out-of-pocket if they wish to try them. Table 10 below describes some supplements used for insomnia, GAD, PD and OCD.

TABLE 10: HERBAL SUPPLEMENTS FOR INSOMNIA, GAD, PD AND OCD

Insomnia			
Supplement	**Dose Range**	**Efficacy**	**Comments**
Melatonin	1-6mg	Best evidence for sleep disturbances due to jet lag	Works best if combined with exposure to sunlight during the day
Valerian Root	400-900mg	Frequently studied with conflicting results	Daytime sleepiness; vivid dreams; may have BZD-like withdrawal symptoms with chronic use
L-tryptophan	1-4 gm	Two out of three published studies showed positive outcomes for sleep	Stomach upset
Generalized Anxiety Disorder			
Supplement	**Dose range**	**Efficacy**	**Comments**
Chamomile	1100mg/day	One small randomized trial showed modest efficacy (p =0.047) in mild to moderate GAD.	Well tolerated, though allergies and anaphylaxis reported
Kava	125-250 mg/day	Number of studies found in favor of kava over placebo in anxiety, but results are not consistent.	**Hepatotoxicity,** sedation, tremors, ataxia, visual disturbance, mild euphoria, urinary retention, scaly skin rash with heavy use
L-theanine	200-400mg/day	May provide relief of anxiety symptoms in psychotic disorders, but no evidence to support use in GAD.	Well tolerated
Panic Disorder			
Supplement	**Dose range**	**Efficacy**	**Comments**
Inositol	12-20gm/day	Limited evidence from 2 small studies.	Flatulence, mania
Obsessive-Compulsive Disorder			
Supplement	**Dose range**	**Efficacy**	**Comments**
Inositol	18gm/day	Limited evidence as monotherapy; No evidence for additional benefit as augmentation to SSRI treatment.	Flatulence, mania
N-acetyl cysteine	1200-2400mg/day	Limited evidence from small randomized controlled trial suggest tolerability and efficacy for adjunct treatment.	Well tolerated
Valerian Root	765mg/day	Superior to placebo as monotherapy in one small study.	Somnolence, vivid dreams; may have BZD-like withdrawal symptoms with chronic use

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