



**City and County of San Francisco**  
**Mayor Gavin Newsom**

Department of Public Health

Community Behavioral Health Services  
1380 Howard Street 5<sup>th</sup> Floor  
San Francisco, CA 94103

**GUIDELINES FOR THE USE OF PSYCHOACTIVE MEDICATIONS IN INDIVIDUALS  
WITH CO-OCCURRING SUBSTANCE USE DISORDERS**

San Francisco Community Behavioral Health Services

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*Portions of these Guidelines have been adapted from the County of Los Angeles- Department of Mental Health, Office of the Medical Director, Parameters for the use of psychoactive medications in individuals with co-occurring substance abuse*

## I. INTRODUCTION

- The purpose of this document is to identify specific clinical policies and procedures and provide a foundation for quality management relating to the use of major classes of psychoactive medications in individuals with co-occurring disorders (CODs) of substance use and mental illness.
- This document is not a comprehensive treatment guideline for the use of psychopharmacologic medications, nor a guideline for the psychopharmacologic treatment of substance abuse. Such guidelines exist, and should be familiar to clinicians, these include:
  1. The Expert Consensus Practice Guideline for Treatment of Schizophrenia;
  2. The APA Guidelines for Treatment of Schizophrenia and Mood Disorders;
  3. The PORT Schizophrenia Guidelines;
  4. The Texas Medication Algorithm Project;
  5. The International Psychopharmacological Algorithm Project Report;
  6. The AHCPH Guidelines for Depression in Primary Care;
  7. The ASAM guidelines for treatment of substance abuse; and
  8. The CSAT guidelines for treatment of substance abuse.
- This guideline represents the consensus among CBHS clinicians and experts in psychopharmacology and substance abuse treatment.
- This guideline in no way substitute for the consumer/physician dialogue and respect for consumer choice that is at the core of sound clinical practice.
- This guideline is designed to encourage consultation, treatment, and monitoring at CBHS clinical sites and departmental education and training.
- This guideline reflects current interpretation of best practices. They will invariably change as new information and medications become available.

## II. GENERAL RECOMMENDATIONS

- When mental illness and substance use disorders co-exist, each disorder is “primary,” requiring integrated, properly matched, diagnosis specific treatment of adequate intensity. Thus, in general, psychopharmacologic interventions are designed to maximize outcome of two primary disorders, as follows:
  - For diagnosed psychiatric illness, the individual receives the most clinically effective psychopharmacologic strategy available, regardless of the status of the comorbid substance disorder. Special considerations apply for utilization of potentially addictive medications that may have psychiatric indications.

- For diagnosed substance disorder, appropriate psychopharmacologic strategies (i.e disulfiram, buprenorphine) may be used as ancillary treatments to support a comprehensive program of recovery, regardless of the status of the comorbid psychiatric disorder.
- Assessment of individuals with CODs should take into account the potential contribution of substance-induced psychiatric disorders to presenting symptoms. Re-assessment of diagnosis and treatment should occur regularly, particularly after a period of abstinence from the abused substance(s).
- Psychoactive medications being taken on an ongoing basis for treatment of a psychiatric disorder should be continued during detoxification from abused substances, unless specific contraindications to the use of these medications exist.
- Assessment for possible pharmacologic treatment of individuals with an exacerbation of psychiatric symptoms during detoxification from abused substances should explicitly consider adjustment of the dose of withdrawal medications prior to addition of other psychoactive medications.
- Assessment for prescription of additional medications for psychiatric symptoms during detoxification should explicitly consider the potential interactions with the withdrawal medications, with the abused substance, and with any associated physiologic complications.
- Psychoactive medications with a low potential for abuse should be preferentially prescribed in individuals with comorbid substance abuse disorders.
- Medications for the treatment of psychiatric disorders should not be withheld from individuals with substance abuse disorders solely because they continue to abuse substances. Rather, the medication treatment regimen should be one that best manages the psychiatric disorder while minimizing the potential for interactions among the prescribed medication, the abused substance, and associated mental and physiologic effects.
- Laboratory studies for assessment of physiologic processes that may be affected by abused substances and are relevant to the metabolism of prescribed psychoactive medications should be obtained, monitored, and documented.
- Individuals with substance abuse disorders should be regularly queried about their degree of adherence to medication regimens, and motivational enhancement techniques should be employed to encourage the appropriate use of medication as well as reduction in substance related harm.

### **III. USE OF ANTIPSYCHOTICS**

- As a general principle, in patients with psychotic presentations, with or without active substance dependence, initiation of treatment for psychosis is generally urgent.
- The atypical antipsychotic medications such as risperidone, olanzapine, quetiapine, ziprasidone, and aripiprazole are the first-line medications for patients with newly diagnosed psychotic disorders and for all co-occurring disorder patients requiring antipsychotic treatment. Atypical antipsychotics are preferred because they are less likely to cause dysphoria, extrapyramidal symptoms, and increased drug cravings that have been associated with typical antipsychotics. Although not a first-line treatment, clozapine has been the most extensively studied antipsychotic in patients with co-occurring disorders. Studies conducted with clozapine have demonstrated increased rates of abstinence and decreased substance use with treatment. Similar (however limited and sometimes discrepant) results have been demonstrated with other atypical agents.
- Antipsychotic medications can be used effectively to treat both acute psychosis and mania. The lowest possible effective dosage should be used, with side effects closely monitored, and the patient should be frequently reevaluated. Abuse of antipsychotic medications, even among substance abusers is rare.
- Antipsychotic medications should be administered concurrently with any withdrawal medications during detoxification of individuals with psychotic disorders who are experiencing psychosis. This may include psychosis associated with delirium.
- Antipsychotic medication regimens prescribed for the emergence of psychotic symptoms or agitation during withdrawal should be re-evaluated after detoxification is completed.
- Depot antipsychotic medication should be preferentially considered in individuals with substance abuse who have a high probability of nonadherence with oral medication regimens.

### **IV. USE OF MOOD STABILIZERS**

- Divalproex should be used preferentially over lithium considering improved adherence, tolerability, and the higher prevalence of mixed states and rapid-cycling in individuals with comorbid substance abuse and bipolar disorder.
- Recognizing that special attention must be directed toward ensuring normal liver function, in individuals with alcohol addiction, divalproex should be used with great caution when liver transaminase levels are greater than twice the upper limit of normal. This value should be monitored on a regular basis.
- Lithium must be monitored carefully in patients at risk for dehydration (due to substance use or other factors) or with concurrent medical illness.

- Carbamazepine is also useful for mood stabilization. Carbamazepine may induce liver enzymes causing a more rapid metabolism of methadone and other drugs leading to withdrawal symptoms.
- Lamotrigine is a well-tolerated mood stabilizer with particular benefit demonstrated in the depressed phase of bipolar disorder. Improvements in mood symptoms and drug craving have been seen when used in bipolar patients with cocaine dependence.
- Gabapentin has been suggested as a mood stabilizer but no controlled studies have demonstrated its effectiveness.
- Patients with co-occurring disorders may be refractory to monotherapy and require use of multiple mood stabilizers or adjunctive use of atypical antipsychotics.

## V. USE OF ANTIDEPRESSANTS

- Psychotropic medications, particularly for mood and anxiety disorders, should be clearly directed to the treatment of known or probable psychiatric disorders, not to medicate feelings. It is important to communicate to patients with addiction that successful treatment of a comorbid anxiety or mood disorder is not intended to remove normal painful feelings associated with unpleasant life experiences. The medication is meant to help the patient experience his or her feelings more accurately, facilitating the process of developing healthy capacities to cope without using substances.
- Data suggests that selective serotonin reuptake inhibitors (SSRIs) and serotonin and norepinephrine reuptake inhibitors (SNRIs) may reduce depressive symptoms and improve quality of life even in patients with CODs who continue to use substances. Furthermore, SSRIs have been demonstrated to be associated with lower alcohol use in a subset of alcohol dependent patients with or without depression. Because newer antidepressants are associated with fewer serious adverse effects, these medications should be preferentially used for treatment of primary mood disorders in individuals with co-occurring disorders. Because of induction of hepatic microsomal activity by alcohol, higher doses of both SSRIs and SNRIs may be considered in individuals with alcohol dependence and major depressive disorders who do not respond to standard doses.
- Bupropion is generally safer in overdose in comparison to tricyclic antidepressants (TCAs), however it is not as safe as SSRIs. Bupropion's mild stimulant and anti-craving properties may make it a useful agent for treating depression in patients with stimulant (or nicotine) abuse. Bupropion may be beneficial in patients for whom use of substances is tightly integrated with sexual activity and expression. The use of drugs that impair performance (SSRIs, SNRI's, TCA's, etc.) only exacerbate anxiety around sex and thus make the individual more likely to relapse on stimulant use. There is a lower incidence of sexual adverse effects with bupropion than with other antidepressants. Bupropion may have utility as an off label treatment for Attention

Deficit Disorder. Bupropion may increase the risk of alcohol withdrawal seizures. Patients who abuse alcohol should be monitored closely.

- Mirtazapine is sedating and associated with weight gain, but has few adverse sexual effects and is generally safe in an overdose.
- TCAs are generally not addictive, but they do have a number of troublesome side effects. Some of these side effects may be additive or synergistic with some of the effects of abused substances (e.g sedation, impaired cognition). Such side effects may be offset by low dosages. Because of induction of hepatic microsomal activity by alcohol, higher doses of TCAs may be considered (with close monitoring) in individuals with alcohol dependence and major depressive disorders that do not respond to standard doses. All of the TCAs are lethal in overdose and should not be given to unmonitored suicidal patients. Because of the potential for cardiotoxicity and arrhythmias in individuals who abuse cocaine, TCAs should generally be avoided in such cases.
- Monoamine oxidase inhibitors (MAOIs) should be avoided in patients with co-occurring disorders unless all other treatments fail. Use of these medications carries the potential for lethal interactions with other drugs including drugs of abuse, e.g. amphetamine, cocaine, ephedrine, ecstasy, dextromethorphan, meperidine, and tap beer.

## VI. USE OF SEDATIVE/HYPNOTICS

- The assessment and pharmacologic treatment of anxiety in individuals with comorbid substance abuse must take into account special considerations, including:
  - The increased possibility that a prescribed anxiolytic medication may be misused or abused.
  - The contribution of the abused substance to the anxiety symptoms through intoxication and withdrawal.
  - Individuals in early recovery have great difficulty regulating medication; fixed dose regimens, not PRNs, are recommended in the treatment of mood and anxiety disorders.
  - The interactions among the abused substance, the metabolic changes resulting from the abused substance, and the prescribed anxiolytic medication.
- Newer antidepressants (e.g. SSRIs, SNRIs, mirtazipine) should be preferentially used for pharmacological treatment of chronic anxiety disorders in individuals with comorbid substance use because of data that suggests symptom reduction and fewer untoward effects relative to TCAs and MAOIs
- Buspirone may be considered because of its relative safety and lack of potential for abuse. Anxiety symptom reduction with buspirone in patients with co-occurring

disorders is limited. Buspirone is not effective for treatment of acute anxiety or panic.

- For pharmacologic treatment of insomnia due to an anxiety disorder in individuals with comorbid substance abuse, sedating non-TCA antidepressants (e.g., trazodone, mirtazapine) should be used preferentially over sedating TCAs due to their relative safety.
- Trazodone is an alternative sedative hypnotic to potentially dependence producing agents. Trazodone has no known abuse potential and low risk of adverse effects. Priapism is an extremely rare (<1 in 4,000) but serious adverse effect to trazodone that requires immediate medical attention.
- Hydroxyzine, diphenhydramine and other sedating antihistamines can be useful for their sedative/hypnotic properties. These medications are generally not abuseable. While not a contraindication, some patients do get a “buzz” from the anticholinergic side effects and may overuse these medications.
- Sedating antipsychotic medications should be used only in the presence of psychotic or manic symptoms, never for anxiety or insomnia alone.

## **VII. USE OF BENZODIAZEPINES**

- Benzodiazepines prescribed as withdrawal medications during detoxification from abused substances should be discontinued after the detoxification period is completed.
- Use of benzodiazepines for treatment of primary anxiety disorders or adjustment disorders should be avoided in individuals with comorbid substance abuse because of their increased potential for abuse.
- In cases when benzodiazepines are the only effective treatment for otherwise unmanageable anxiety, those with especially rapid onset (e.g. alprazolam and diazepam) should be avoided in order to minimize the potential for abuse. There is evidence to suggest that benzodiazepines slow to cross the blood-brain barrier or with longer half-lives may have a lessened potential for abuse. Therefore, less frequently used benzodiazepines such as chlordiazepoxide and oxazepam may appear more favorably.
- Benzodiazepines are the recognized treatment of choice for the management of alcohol withdrawal. Agitation, and/or delirium stemming from alcohol withdrawal should be treated in an inpatient or medically monitored setting

## VIII. USE OF PSYCHOSTIMULANTS

- A thorough psychiatric evaluation of a patient reporting symptoms of a co-occurring substance abuse disorder and attention deficit disorder is essential. ADHD in adults is virtually always preceded by symptoms in childhood. These symptoms may or may not have been recognized as ADHD.
- Psychostimulants are very effective in children and may be effective in adults. Psychostimulants have a high potential for abuse and dependence. They should generally be avoided in patients with a history of psychostimulant abuse. Methamphetamine (Desoxyn®) carries the highest abuse potential and offers no therapeutic advantage over other amphetamine derivatives, thus should never be used in patients with co-occurring disorders. Once-daily long acting preparations of methylphenidate or amphetamine are preferred to limit euphoric effects of immediate drug release. The commercial methylphenidate preparation Concerta® may have a lower risk of abuse than other formulations and should be considered in patients who crush or chew long acting preparations for immediate release effects.
- Psychostimulants are useful for treatment refractory depression with severe psychomotor retardation and apathy. In patients with co-occurring disorders, these should not be used until other medications and augmentation strategies have failed. They should not however be withheld solely because of a patient's substance use disorder history.
- If psychostimulants are prescribed to an outpatient, prescriptions should be written for limited quantities and compliance closely monitored for overuse or diversion.
- Alternatives exist for the treatment of attention deficit symptoms. Atomoxetine is a non-stimulant medication approved for the treatment of attention deficit disorder in adults. Atomoxetine does not appear to have significant potential for abuse. Noradrenergic tricyclic antidepressants (e.g. desipramine) and bupropion have been shown to be effective for attention deficit disorder in adults. Bupropion is better tolerated and safer to use than TCAs.

## IX. MEDICATIONS FOCUSED ON SUBSTANCE USE

### Alcohol Addiction:

#### Disulfiram:

- The first drug that was approved for treatment of alcohol abuse, disulfiram, may be used for the prevention of relapse in patients with comorbid alcohol abuse. This is a medication that does not specifically block craving, although, if taken regularly, it may simplify the daily struggle against urges toward alcohol. If the patient takes a drink, disulfiram causes a very unpleasant flushing reaction. In large randomized

controlled trials, disulfiram has not been effective, however mostly due to lack of medication adherence. In situations where it can be prescribed with daily monitoring of ingestion, it can be useful. Prescribers must also consider the ethical issues of prescribing a “punishment” (punishment as classically defined in conditioning studies) in a patient who is likely to use alcohol despite taking disulfiram. Disulfiram should be used with caution in patients with co-occurring psychotic disorders and substance abuse. Such patients should be evaluated for disulfiram-induced exacerbation of psychosis or mania.

Naltrexone:

- Naltrexone is a model anti-craving medication. Naltrexone was initially applied to alcoholics because of animal studies showing that alcohol activated the endogenous opioid system. Naltrexone consistently reduces alcohol consumption in animal models. In humans, controlled trials have consistently found that patients who were randomly assigned to naltrexone had significantly fewer relapses than placebo treated patients. Naltrexone has been reported to suppress craving compared to placebo.

Acamprosate:

- In addition to naltrexone, acamprosate was approved for the treatment of alcoholism in 2004. Acamprosate has multiple actions that may play a role in the reduction of alcohol use and cravings. TID dosing may limit its utility, particularly in a more impaired population. Acamprosate’s effects on cravings do not directly involve the endogenous opioid system, therefore the combination of naltrexone and Acamprosate may have additive benefit. This combination showed increased efficacy in one European trial and is currently being studied in the U.S. Acamprosate should be considered in individuals with alcohol abuse for whom naltrexone is not tolerated, or in combination with naltrexone when naltrexone alone is not effective

Cocaine Addiction:

Disulfiram:

- Disulfiram may also reduce the frequency of cocaine use even among patients who do not use alcohol. The mechanism by which disulfiram is helpful in patients suffering from cocaine abuse is unknown.

Modafinil:

- Modafinil has been found in two trials (one open trial, one randomized controlled trial) to reduce the “high” and reduce cravings from cocaine. While this medication was well accepted by patients, the medication was not reported to produce euphoria and there has been no indication of excessive use or abuse in clinical trials.

Opioid Addiction:

Methadone (agonist therapy):

- Methadone maintenance is offered in the context of narcotic treatment programs, which may offer ancillary services such as individual/group counseling, primary care/HIV treatment, and psychiatric evaluation and treatment. When used at flexible doses, methadone has been associated with superior treatment adherence compared to buprenorphine. Methadone is possibly more effective at preventing heroin use than buprenorphine particularly at higher doses of methadone. There is a possible dose-related reduction in mortality associated with methadone therapy. There is insufficient evidence to determine if methadone is superior to buprenorphine considering criminal activity or quality of life. Methadone's utility is restricted by daily dosing at a narcotic treatment program.

#### Buprenorphine (partial agonist therapy):

- Buprenorphine is administered in office-based medical practices such as primary care clinics. This offers the benefit of a de-stigmatized opioid dependence treatment, enhanced privacy, and improved access to primary care treatment. Buprenorphine can be dispensed from community pharmacies. In stabilized patients, visits can be at intervals up to 30 days. Buprenorphine is associated with milder withdrawal symptoms, lower risk of overdose, and lower risk of clinically significant drug-drug interactions than methadone. Synergistic CNS depression and death are possible when buprenorphine is used in combination with other CNS depressants (e.g. benzodiazepines, alcohol, barbiturates).

#### Naltrexone (antagonist therapy):

- Naltrexone is a less stigmatized treatment option for opioid dependence compared to agonist therapy. Naltrexone elicits withdrawal in patients who are opioid dependent, thus complete abstinence must be obtained for up to 2 weeks before naltrexone can be initiated. Withdrawal symptoms and cravings often result in relapse before treatment can be started. Naltrexone's lack of opioid agonist effects often yields low incentive for acceptance and adherence to treatment. Naltrexone may be associated with a higher risk of overdose death if relapse occurs. Naltrexone's role in therapy may be restricted to a subgroup of individuals with strong motivation and psychosocial support.