BHMEDS

Behavioral Health Medications

- Generic and Brand Medication Names
- Purpose
- Usual Dose and Frequency
- Potential Side Effects
- Emergency Conditions
- Cautions
- Substance Use Disorders Treatment Medications

Mid-America (HHS Region 7)
ATTC Addiction Technology Transfer Center Network
Funded by Substance Abuse and Mental Health Services Administration

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9th Edition 2014

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This Publication is available for free download via the Mid-America ATTC Web site at ATTCnetwork.org/midamerica.

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About this Publication

Originally developed as a companion piece to the Mid-America ATTC systems change curriculum, *A Collaborative Response: Addressing the Needs of Consumers with Co-Occurring Substance Use and Mental Health Disorders*, this edition includes adaptations made for inclusion in CSAT's *TIP 42: Substance Abuse Treatment for Persons with Co-Occurring Disorders*. The language has been modified to increase readability for a larger audience and, in keeping with the goal of updating the publication biannually, several new medications are included.

COUNSELORS' USE OF THIS PUBLICATION

A list of generic and brand names is included for the following medications:

- Antipsychotics/Neuroleptics
- Medication-Induced Symptoms Treatment
- Antimanic Medications/Mood Stabilizers
- Antidepressant Medications
- Antianxiety Medications
- Stimulant Medications
- Narcotic and Opioid Analgesics
- Hypnotics (Sleep Aids)
- Substance Use Disorders Medications
    - Alcohol
    - Opioids
    - Tobacco
    - Others

Each section includes the following topics for the different medication types:

Purpose: Describes typical uses of medications, including specific symptoms treated and positive treatment response expected.

Usual dose, frequency, and side effects: Discusses when and how medications are administered, typical side effects, and methods for monitoring side effects.

Potential side effects: Lists common side effects.

Potential for abuse or dependence: Elaborates upon those medications with potential for abuse and/or physical dependence. Discusses withdrawal reactions and management of withdrawal.

Emergency Conditions: Includes risks associated with overdose, withdrawal or other medications' reactions.

Cautions: Describes risks associated with use of additional medications (i.e., over the counter), increasing or discontinuing use of medications, and adverse consequences with concurrent use of alcohol and/or street drugs.

Special Considerations for Pregnant Women: Describes risks for pregnant women prescribed psychotherapeutic medications. References to research are included. The role of practitioners in encouraging discussion between patients and/the prescribing physician is emphasized.

IMPORTANT NOTES ACROSS MEDICATION TYPES

Name brand medications have a limited patent. When the patent expires, the medication may be made as a generic. The generic name of a medication is the actual name of the medication and never changes. A generic medication may be made by many different manufacturers. Additionally, manufacturers can make several forms of a single medication with only slight variations. For instance, they may vary the color, size, or shape of the medication. If a person says his or her medication "looks different" AND he or she is experiencing new side effects, contact the prescriber immediately.

For ease of reading, some technical terms are defined in accompanying footnotes. All medications are listed in the index along with page numbers for quick reference. When specific brands are discussed in the accompanying text, the name of the medication is **bolded** to assist the reader in finding the reference.

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LIMITATIONS OF THE PUBLICATION

This publication is designed as a quick "desk reference" for substance use disorder and mental health treatment providers. It is not intended to be used as a complete reference for psycho-therapeutic medications. The section, "Tips for Communicating with Physicians," is meant to be just that: tips for communicating. The publication assumes providers are knowledgeable about the Health Insurance Portability and Accountability Act (HIPAA) regulations, including issues related to privacy and confidentiality and will use these communication tips in accordance with those regulations. For more information about HIPAA, refer to the SAMHSA Web site: www.samhsa.gov/healthprivacy.

The section, "Talking with Clients about their Medication," is a prompt designed to help the provider initiate conversation about medication management and adherence with clients who have co-occurring mental health and substance use disorders. It is not intended as a complete guide to client education. For a more thorough discussion of these co-occurring issues, see the current edition of the American Society of Addiction Medicine's (ASAM's) *Principles of Addiction Medicine*, Fifth Edition (ASAM 2014).

For physicians desiring a more in-depth discussion regarding the challenges of treating specific population groups with substance use disorders (e.g., homeless, older adults, people with HIV/AIDS or hepatitis, pregnant or nursing women, etc.), which include medication compliance, adverse drug interactions, and relapse with the use of potentially addictive medications, refer to the current edition of the American Society of Addiction Medicine's (ASAM's) *Principles of Addiction Medicine*, Fifth Edition (ASAM 2014), and CSAT's *TIP 42: Substance Abuse Treatment for Persons with Co-Occurring Disorders* (CSAT 2005).

Antipsychotics/Neuroleptics

GENERIC	BRAND
Conventional Antipsychotics / First Generation Antipsychotics (FGA)	
chlorpromazine	Thorazine
fluphenazine	Prolixin, Permitil, Anatensol, Prolixin Decanoate
haloperidol	Haldol, Haldol Decanoate
loxapine	Loxitane
mesoridazine	Serentil
molindone	Moban
perphenazine	Trilafon
pimozide	Orap
thioridazine	Mellaril
thiothixene	Navane
trifluoperazine	Stelazine
Novel /Atypical Antipsychotics / Second Generation Antipsychotics (SGA)	
asenapine	Saphris
clozapine	Clozaril, Fazaclo
iloperidone	Fanapt
olanzapine	Zyprexa, Zyprexa Zydis
paliperidone	Invega, Invega Sustenna
quetiapine	Seroquel, Seroquel XR
risperidone	Risperdal, Risperdal Consta
ziprasidone	Geodon
lurasidone	Latuda
Atypical Antipsychotics – Third Generation Antipsychotics (TGA)	
aripiprazole	Abilify, Abilify Discmelt

PURPOSE

Antipsychotics (neuroleptics) are most frequently used for persons who experience psychotic symptoms as a result of having some form of schizophrenia, severe depression or bipolar disorder. They may be used to treat brief psychotic episodes caused by drugs of abuse. Psychotic symptoms may include being out of touch with reality, "hearing voices," and having false perceptions (for example, thinking you are a famous person, thinking someone is out to hurt you, etc.). Antipsychotic medications can be effective in either minimizing or stopping these symptoms altogether. In some cases, these medications can shorten the course of the illness or prevent it from happening again.

Positive treatment response to antipsychotic medications allows many with severe and disabling mental disorders to live and function in the community, often relatively normally. This positive response may include thoughts that are more rational, decreased psychosis[1], paranoia and delusions, behavior that is more appropriate, and the ability to have relationships and work.

All of the older and newer antipsychotic medications are approved by the Food and Drug Administration (FDA) and are thus evidence-based treatments (EBT) for schizophrenia. The newest antipsychotic medications—**Risperdal, Saphris, Fanapt, Zyprexa, Seroquel, Geodon**, and **Abilify**—show positive effects across a range of disorders. These medications stabilize mood and are also used to treat bipolar disorder. Aripiprazole and quetiapine are used adjunctively to treat depression. Trifluoperazine can be used short term as an anxiolytic. A growing number of the atypical antipsychotic medications have received FDA approval for treatment of bipolar illness. Aripiprazole, olanzapine, quetiapine,

[1] *psychosis*: a mental disorder characterized by distinct distortions of a person's mental capacity, ability to recognize reality, and relationships to others to such a degree that it interferes with that person's ability to function in everyday life.

risperidone (injectable) and ziprasidone are FDA approved for use in bipolar maintenance therapy (Stahl, 2011, p. 698).

USUAL DOSE, FREQUENCY & SIDE EFFECTS

All medications have specific doses and frequencies. Early "acute" symptoms may be treated with higher doses of medication, and then reduced after stabilization has occurred (Kreyenbuhl et al., 2009). The physician will specify the exact amount of medication and when it should be taken. This information is on the prescription bottle. Many medications are taken once a day, some at bedtime to take advantage of the drowsiness side effect of some antipsychotic medications. Several medications are taken in pill form or liquid form. Others are given by injection once or twice per month to ensure that the medication is taken reliably. It is important to take medications on schedule. It is also important that people talk to their doctor so they know about potential side effects and steps they need to take to monitor their health.

Atypical antipsychotics are different from conventional antipsychotics. They work on both the positive and negative symptoms of schizophrenia by affecting dopamine and serotonin neurotransmitter pathways. Hence, they have been FDA approved for use in depression as well, where serotonin pathways are affected. Also, because the atypical antipsychotics work in a slightly different way than traditional antipsychotics, they are less likely to produce serious side effects, such as tardive dyskinesia[2] or neuroleptic malignant syndrome[3].

The side effects of antipsychotic medications vary among individuals, and can often be unpleasant to endure and lead to patients choosing to discontinue their medication. The most common symptoms include sedation[4], hypotension (decreased or lowered blood pressure), anticholinergic effects (such as dry mouth, urinary hesitancy or retention, constipation and visual disturbance), sexual dysfunction, and extrapyramidal symptoms (EPS) (see the Potential Side Effects section on page 8 for more information about EPS). Other side effects include hyperprolactinemia (an elevated level of prolactin in the blood that leads to the production of breast milk) which has been seen in risperidone and ziprasidone; cardiac arrhythmia (an irregular heartbeat or abnormal heart rhythm that can produce symptoms such as palpitations, dizziness, fainting, shortness of breath and chest discomforts), seen in ziprasidone and thioridazine; and agranulcytosis, which has been noted in the use of clozapine (Stahl, 2008, p.400-401).

Metabolic syndrome issues, including weight gain, hyperglycemia (elevated blood sugar), and dyslipidemia (an abnormal amount of lipids [cholesterol and/or fat] in the blood) are seen in both FGA and SGA antipsychotics. The greatest risks tend to fall with the use of clozapine and olanzapine, intermediate risk is seen with quetiapine. Aripiprazole, risperidone, and ziprasidone present the lowest risk of metabolic syndrome. The most common mild side effects are either sedation or agitation, especially when starting the medications. The most worrisome side effects are weight gain and elevated blood sugar and lipids[5]. There is also some evidence that the use of atypical antipsychotics may lead to the development of diabetes mellitus[6] (Sernyak

[2] *tardive dyskinesia*: A central nervous system disorder characterized by twitching of the face and tongue, and involuntary motor movements of the trunk and limbs; occurring especially as a side effect of prolonged used of antipsychotic medications.

[3] *neuroleptic malignant syndrome*: A very rare but life-threatening neurological disorder most often caused by a reaction to antipsychotic/neuroleptic medications. Typically developing within the first two weeks of treatment; but can develop at any time. The syndrome can also occur in people taking antiparkinsonian medications if discontinued abruptly.

[4] *sedation*: Inducing a relaxed easy state especially by the use of sedatives (drugs).

[5] *lipids*: Any of various substances including fats, waxes, and phosphatides that with proteins and carbohydrates make up the principal structural components of living cells.

[6] *diabetes mellitus*: An endocrine disorder in which insulin is inadequately secreted or used by the body.

et al., 2002). Because diabetes is associated with obesity, it is unclear whether the diabetes is actually caused by certain atypical antipsychotic medications or obesity. These issues can be medically worrisome and lead to patients choosing to discontinue their medication. In addition, because effectiveness and side effects vary across medications and people, matching the right medication to the right person is imperative to appropriately address these issues.

Clozapine can very rarely cause serious abnormalities or irregularities in the blood cells (blood dyscrasias[7]). As such, those taking clozapine are entered into a "Clozapine Registry" (TEVA Clozapine Patient Registry). TEVA is the largest generic medications manufacturer. The Registry is a systematic active post-marketing surveillance program mandated by the Food and Drug Administration (FDA). Under this mandate, TEVA program administrators are required to register patients, physicians and pharmacies, collect and monitor white blood cell (WBC) counts and absolute neutrophil count (ANC) values and process adverse events. Approximately 1 to 2% of people who take clozapine develop a condition in which their white blood cell count drops drastically (agranulocytosis[8]). As a result, they are at high risk for infections due to a compromised immune system, and this could be fatal. However, most cases of agranulocytosis can be treated successfully by stopping clozapine treatment. To maintain safety, white blood cell counts must be checked each week for six months. If there are no low counts the patient can be monitored every two weeks for an additional six months. Afterwards, the patient may qualify for every four week monitoring. The results must be sent to the person's pharmacy before he or she can pick up the next supply of medication.

Risperidone and olanzapine came soon after clozapine. Both are classified as "high potency" antipsychotics. Risperidone may cause involuntary movements, tremors, muscular rigidity, and immobility without paralysis, and at higher doses, can have moderate sedative effects. Risperidone is one of the most notorious antipsychotics for causing hyperprolactinemia (abnormally high levels of prolactin in the blood). Some studies have shown that as many as 60% of women and 40% of men have experienced this phenomenon.

Olanzapine is highly sedating and has a higher tendency to cause weight gain and other metabolic changes (Leucht et al., 2013). Metabolic syndrome is a concern with the use of olanzapine. Providers may periodically monitor weight, body mass index (BMI) and waist circumference to evaluate risk.

Risperidone long-acting injection is an injection of microencapsulated[9] medication that releases into the body at a constant level. An injection is usually given every two weeks. Side effects are similar to those for risperidone.

Quetiapine has antipsychotic properties at higher doses, and antidepressant properties at lower doses. It is used in the acute and maintenance phases of both schizophrenia and bipolar illness, and bipolar depression. It is very sedating and calming at moderate to high doses. In some prison settings, there have been reports of "abuse" of both quetiapine and olanzapine, by prisoners feigning psychotic symptoms in order to obtain heavy sedation (Bogart & Ott, 2011).

[7] *blood dyscrasias*: A disease of the blood usually involving cellular abnormalities (i.e., poorly functioning or fewer than normal platelets, or loss of certain blood proteins called "clotting factors"; poorly functioning or decreased numbers of red and/or white blood cells).

[8] *agranulocytosis*: A condition in which there are too few of a specific type of white blood cell called neutrophils in the blood. Affected people are susceptible to infections.

[9] *microencapsulated*: To ensure in a tiny capsule material (as a medicine) that is released when the capsule is broken, melted, or dissolved.

Ziprasidone and aripiprazole are newer agents and have only moderate sedative and few weight, diabetes, or lipid effects, but their antipsychotic response seems to be less predictable. Ziprasidone has also been linked to a serious heart condition called "torsades de pointes" and sudden cardiac death through its effect on QTc prolongation. This heart condition can lead to dysrhythmias (irregular heart rhythms) which need to be treated quickly to prevent serious complications. The likelihood of this heart condition is low, but should be looked at by the doctor when beginning treatment with ziprasidone. Providers should order an EKG (electrocardiogram) in those with preexisting heart conditions and weigh the risk of use. A doctor or pharmacist should review the medications a patient is taking to check for medication interactions.

Paliperidone and iloperidone are other antipsychotics and they are related to risperidone. Both medications cause moderate sedation and weight gain. Paliperidone can cause dose-dependent EPS (various movement disorders), hyperprolactinemia (an elevated level of prolactin in the blood), and dyslipidemia (an abnormal amount of lipids [cholesterol and/or fat] in the blood). Iloperidone may also cause dyslipidemia and orthostatic hypotension (a form of low blood pressure that happens when you stand up from sitting or lying down; it can make you feel dizzy or lightheaded, and maybe even faint).

Paliperidone metal tablets provide 24 hours of medication for the patient. Paliperidone long-acting injections are also available for patients that are stable on paliperidone. This long-acting injection provides an entire month's worth of medication in a single shot and can be useful for patients that don't always remember to take their medications. Patients should be told that the paliperidone metal capsule will pass with their normal bowel function; this should not be a cause for alarm.

Iloperidone is given twice a day and has a similar action to paliperidone and risperidone.

Asenapine is the newest atypical antipsychotic available in the United States. It's an orally disintegrating tablet that the patient places on the tongue and the tablet will dissolve.

Traditional antipsychotics are cheaper than the newer atypical antipsychotics. On the other hand, the newer antipsychotics, when taken in proper dosage, have generally fewer clinical side effects and a broader treatment response than traditional antipsychotics.

POTENTIAL SIDE EFFECTS

Extrapyramidal symptoms (EPS) are a constellation of symptoms that can be experienced by people taking antipsychotic medications. They are a collection of abnormal movements effecting voluntary muscles and coordination of the neck, spine, gait/walking, oral/facial, fingers, limbs, and eyes as well as associated vocalizations, breathing and swallowing. There are four main types of EPS: pseudoparkinsonism, akathisia, acute dystonia, and tardive dyskinesia. The onset of these side effects is often seen within the first few weeks of treatment. The first three of the four main types of EPS listed above are typically reversible.

Tardive dyskinesia is a potentially irreversible side effect of antipsychotic medications. It is seen in those who have had long-term exposure to high doses of FGA. Symptoms include oral/facial movements, lip smacking, and tongue thrusting, body jerks, spastic muscle contractions and/or stiffness and tics. Caught early in treatment, this condition may be reversible.

EPS can occur with both therapeutic and toxic doses of antipsychotics and may occur after any dosage change/cessation. They are more common in FGA, but are also seen in high potency SGA. Anticholinergic medica-

tions such as benztropine are used to manage the discomfort associated with EPS.

Metabolic Symptoms - Symptoms of diabetes mellitus (associated with obesity)

Metabolic syndrome describes a group of risk factors that raise your risk for heart disease, diabetes and stroke. Five symptoms contribute to this constellation, and include a large waistline, high triglycerides, low HDL, high blood pressure, and high fasting blood sugar.

Other symptoms include:

- Excessive thirst and hunger
- Fatigue
- Frequent urination
- Headaches
- Slow healing cuts and/or blemishes
- Weight loss

Neuroleptic Malignant Syndrome (very rare)

Neuroleptic malignant syndrome (NMS) is a life-threatening condition that can occur with antipsychotic medications. The use of high-potency antipsychotics, a rapid increase in dose, and use of long-acting forms of medication can increase the risk of developing NMS. Treatment for NMS varies but is generally supportive care and removal of the offending antipsychotic medication. Symptoms of NMS include:

- Blood pressure up and down
- Dazed and confused
- Difficulty breathing
- Muscle stiffness
- Rapid heart rate
- Sweating and shakiness
- Temperature above normal

Other Potential Side Effects

- Blurred vision
- Changes in sexual functioning
- Constipation
- Diminished enthusiasm
- Dizziness
- Drowsiness
- Dry mouth
- Lowered blood pressure
- Muscle rigidity
- Nasal congestion
- Restlessness
- Sensitivity to bright light
- Slowed heart rate
- Slurred speech
- Upset stomach
- Weight gain

Note: Any side effects that bother a person need to be reported and discussed with the prescribing physician. Anticholinergic/anti-parkinsonian medications like benztropine or trihexyphenidyl may be prescribed to control movement difficulties associated with the use of antipsychotic medications.

EMERGENCY CONDITIONS

Contact a physician and/or seek emergency medical assistance if the person experiences involuntary muscle movements, painful muscle spasms, difficulty urinating, eye pain, skin rash or any of the symptoms listed above under EPS, *tardive dyskinesia*, and *neuroleptic malignant syndrome*. An overdose is always considered an emergency and treatment should be sought immediately.

POTENTIAL FOR ABUSE OR DEPENDENCE

The potential for abuse for antipsychotics as a class is relatively low. There are not much data regarding the abuse of traditional antipsychotics currently. One novel antipsychotic that has had reports of abuse is quetiapine (**Seroquel**). People who abuse quetiapine usually crush and "snort" the particles to self-medicate for anxiety and insomnia (Reeves & Brister, 2007). Physical dependence from continued use of these medications across

the class is rare. Withdrawal reactions such as involuntary movements that can last two to four weeks after prolonged use of antipsychotics have been reported. In order to manage these withdrawal reactions, a slow tapering off of the antipsychotics (over four to eight weeks) is recommended. Medications such as benztropine, diphenhydramine and trihexyphenidyl can be used during this taper period to lessen the movement's frequency and severity.

CAUTIONS

- Doctors and pharmacists should be told about all medications being taken and dosage, including over-the-counter preparations, vitamins, minerals, and herbal supplements (such as St. John's wort, echinacea, ginkgo, ginseng, etc.).
- People taking antipsychotic medications should not increase their dose unless this has been *checked with their physician and a change is ordered*.
- Black Box warnings were issued on both first and second generation antipsychotics with regards to use in elderly patients with dementia (A black box warning is the sternest warning by the U.S. Food and Drug Administration [FDA] that a medication can carry and still remain on the market in the United States). An increased risk of death has been associated with their use to control dementia-related behaviors.
- **Clozaril** and **Fazaclo OD** were issued Black Box warnings for agranulocytosis, seizures and myocarditis as well as increased risk of mortality in the elderly.

SPECIAL CONSIDERATIONS FOR PREGNANT WOMEN

For women of childbearing age who may be or think they may be pregnant, the physician should discuss the safety of this medication before starting, continuing, or discontinuing medication treatment. Practitioners may have a role in encouraging this discussion by suggesting their clients talk with the prescribing physician.

Generally, the use of antipsychotic medications should be avoided in the first trimester unless the mother poses a danger to herself, to others, or to the unborn child, or if the mother shows signs of profound psychosis (Cohen, 1989). Tapering and discontinuation of antipsychotic medication 10 days to two weeks before delivery is generally advised, though the way this is done varies by medication (Mortola, 1989).

Haloperidol, thioridazine, fluphenazine, perphenazine, chlorpromazine, and trifluoperazine are some of the antipsychotic medications that have a larger reproductive safety profile. No significant developmental malformations have been documented with chlorpromazine, haloperidol, and perphenazine (ACOG, 2009).

Medication-Induced Symptoms Treatment

GENERIC	BRAND
Anticholinergic agents	
amantadine	Symmetrel
benztropine	Cogentin
diphenhydramine	Benadryl
trihexyphenidyl	Artane

PURPOSE

Symptoms associated with antipsychotic medication use can be very unpleasant. Because of the action of antipsychotics, which cause dopamine and acetylcholine blockade in various regions of the brain, patients can develop extrapyramidal symptoms (EPS). When EPS is noted, providers will reduce the dose of the current medication, stop the medication completely, or switch to a lower potency antipsychotic. If it is necessary to use a medication that has been effective but causes EPS, providers may prescribe additional medications to address these symptoms. Antiparkinsonian (anticholinergic) medications are typically used to control these side effects associated with antipsychotic medications. They are called antiparkinsonian because the neurological side effects of antipsychotic medications are similar to the symptoms of Parkinson's disease (such as, tremors, stiff or rigid muscles, poor balance, a distinctive unsteady walk, etc.).

Although the medications most commonly used to address EPS consist of anticholinergic and antihistaminergic medications, benzodiazepines, beta-adrenergic antagonists (propranolol), beta-adrenergic agonists (clonidine), or dopamine agonists (amantadine) may also be used (Mueser, & Jeste, 2008).

Anticholinergics can be given either orally or intramuscularly for more severe forms of extrapyramidal side effects, such as acute oculogyric crises (eyes rolling back in the head accompanied by posturing) or dystonias (prolonged and unintentional muscular contractions of voluntary or involuntary muscles) which impair a patient's breathing. Trihexyphenidyl and benztropine are the most common anticholinergic medications given to control EPS (Kamin, Manwani, & Hughes, 2000).

Benzodiazepines, beta-adrenergic antagonists, and beta-adrenergic agonists are usually used for akathisia (restlessness, rocking, and fidgety feeling) (Kamin, Manwani, & Hughes, 2000).

The dopamine reuptake inhibitor amantadine can also be used for symptoms related to medication induced Parkinsonism (tremor, rigidity, slow movement).

Providers will periodically assess patients for involuntary movements associated with antipsychotic medication use. Patients should report any new symptoms associated with antipsychotic medication as soon as they occur. Acute extrapyramidal side effects tend to resolve rapidly when noted and promptly addressed.

It is important to note that the antiparkinsonian medications listed in this section are only those used in the management of the side effects of antipsychotic medications. There are other medications used to treat primary Parkinson's disease that are not discussed in this section because those medications are currently not used for the management of side effects related to antipsychotics. If you would like more information on Parkinson's disease, talk with your doctor or pharmacist.

USUAL DOSE & FREQUENCY

All medications have specific doses and frequencies. The physician will specify the exact amount of medication and when it should be taken. This information is on the prescription bottle. These medications have very specific doses and taking too much can be harmful. A doctor must be consulted in order to safely change the dose in response to side effects of the antipsychotic medications.

POTENTIAL SIDE EFFECTS

- Constipation
- Dizziness
- Dry mouth
- Heart failure
- Irritability
- Light-headedness
- Stomach upset
- Tiredness

EMERGENCY CONDITIONS

Report immediately any overdose or changes in heart rate and/or rhythm to the doctor.

POTENTIAL FOR ABUSE OR DEPENDENCE

There is not clear evidence on whether these medications could be abused by persons with severe mental illness who require neuroleptics. However, the results of a study from Australia developed by Buhrich et al. (2000) suggest that some of these medications could be abused. Many of the people who abuse/misuse antiparkinsonians in this study used these medications "to get high, to increase pleasure, to decrease depression, to increase energy and to relax" (Buhrich et al., 2000, p. 929). This survey study also found that the misuse of other drugs accompanied the misuse of antiparkinsonian medications. Consequently, in the context of co-occurring mental health and substance use disorders, providers and consumers need to be aware of and openly communicate about the abuse potential of these medications.

CAUTIONS

- Doctors and pharmacists should be told about all medications being taken and dosage, including over-the-counter preparations, vitamins, minerals, and herbal supplements (for example, St. John's wort, echinacea, ginkgo, ginseng, etc.).
- People taking antiparkinsonian/anticholinergic medications should not increase their dose unless this has been *checked with their physician and a change is ordered*.

SPECIAL CONSIDERATIONS FOR PREGNANT WOMEN

The risk of birth defects associated with benztropine, trihexyphenidyl, and diphenhydramine is not clear, although there is some evidence to suggest that amantadine may produce a deformed baby (Mortola, 1989). For all women of childbearing age who may be or think they may be pregnant, the physician should discuss the safety of this medication before starting, continuing, or discontinuing medication treatment. Practitioners may have a role in encouraging this discussion by suggesting their clients talk with the prescribing physician.

Antimanic Medications/Mood Stabilizers

GENERIC	BRAND
Lithium products	
lithium	Eskalith, Eskalith CR, Lithobid, Lithostat, Lithium carbonate tablets, Lithium citrate syrup
Anticonvulsant products[10]	
carbamazepine	Tegretol, Carbatrol, Tegretol XR, Equetro
valproate (valproic acid)	Depakote, Depakote Sprinkle, Depakote ER, Depakene, Stavzor
lamotrigine	Lamictal, Labileno, Lamictin
Atypical antipsychotics	
(see Antipsychotics, p. 8 for side effects)	
aripiprazole	Abilify
asenapine	Saphris
olanzapine	Zyprexa, Zyprexa Zydis
olanzapine plus fluoxetine	Symbyax
quetiapine	Seroquel
risperidone	Risperdal
ziprasidone	Geodon
Other anticonvulsant products (NOT FDA approved for the treatment of bipolar disorder)	
gabapentin	Neurontin
levetiracetam	Keppra, Keppra XR
oxcarbazepine	Trileptal
tiagabine	Gabitril
topiramate	Topamax, Topamax Sprinkle

PURPOSE

Antimanic/mood-stabilizing medications are used to treat symptoms associated with bipolar illness. They are used in acute and maintenance phases to control mania, mood swings, anger or agitation, impulsivity, and suicidal ideation. Mood stabilizers are also used to address symptoms of anxiety and psychotic disorders.

[10] *anticonvulsants*: Usually refers to an agent that prevents or stops *convulsions*; an abnormal violent, involuntary contraction or series of contractions in the muscles.

Bipolar illness is classified into three distinct subtypes: Bipolar I, bipolar II or cyclothymia. The distinctions between each classification relates to the presence of mania, hypomania, and a depressive episode. The duration of symptom presentation is also considered.

Bipolar illness is classically characterized by cycling moods, from severe highs (mania) to severe lows (depression). Hypomania falls somewhere below mania, but considerably above what is "normal" for an individual's baseline temperament. The "highs" and "lows" vary in intensity, frequency, and severity.

A diagnosis of Bipolar I requires at least one full blown manic episode. It could also include the occurrence of a hypomanic and a depressive episode.

Bipolar II requires the presence of a *hypomanic* episode and a current or past major depressive episode. Bipolar II differs from bipolar I in that it does not include a full blown manic episode, but requires a *depressive component* and the lesser hypomanic feature for a diagnosis to be made.

Cyclothymia is a longer version of this mood spectrum disorder. It includes a sub threshold of hypomanic and depressive symptoms over two years that do not reach the level of diagnostic criteria or a Bipolar II diagnosis.

Bipolar cycles that occur more often than three times a year are considered "rapid cycling." This condition is often found in people with higher rates of substance use.

Positive treatment responses to antimanic/mood-stabilizing medications include a decrease in manic symptoms, that is mood stabilization, more organized thought processes, fluent and focused speech, enhanced sleep, cessation of risky behavior,

cessation of suicidal ideation and a return to baseline function.

Left untreated, bipolar mania can progress to a full blown psychotic state. Addressing the symptoms in the acute phases of the illness decreases the likelihood of this occurrence. By leveling mood swings with antimanic medications, suicidal and other self-harming behaviors can be decreased. Additionally, appropriate treatment with antimanic medications can reduce a person's violent outbursts toward others or property.

The following medications are FDA approved for bipolar illness:

Bipolar I: **Depakote**, **Equetro**, lithium; aripiprazole, ziprasadone, risperidone, **Saphris**, quetiapine, **Thorazine**, and alanzapine.

Mixed episodes: **Equetro**, aripiprazole, ziprasadone, risperidone, asenapine, olanzapine.

Maintenance: **Lamictal**, lithium, aripiprazole, olanzapine.

Bipolar II: Quetiapine, **Latuda**, and **Symbyax**, an olanzapine-fluoxetine combination medication is FDA approved for the treatment of bipolar depression.

USUAL DOSE, FREQUENCY & SIDE EFFECTS

All medications have specific doses and frequencies. The physician will specify the exact amount of medication and when it should be taken. This information is provided on the prescription bottle. Most medications in this class are given 2 to 4 times per day. Some extended release formulations[11] may be given every 12 hours. Dosage is determined by the active amount of medication found in the person's blood after taking the medication, and by his or her response to the medication.

Close blood level monitoring is required until the person reaches their optimal dose.

Monitoring Medication Levels: Before beginning treatment with mood stabilizers, the provider may want to order baseline laboratory studies. These can include CBC, kidney function Electrolytes (sodium and potassium), thyroid studies, liver function and a pregnancy test.

Certain mood stabilizers must be monitored periodically to establish therapeutic medication level or possible toxicity. This is often done upon initiation of treatment, when a dose is adjusted or when toxicity is suspected. These include lithium, carbamazepine, and valproic acid.

Lithium has a very narrow therapeutic index and as such, can easily become toxic to patients. Symptoms of lithium toxicity[12] include nausea, diarrhea, shaking of the hands, dizziness, twitching, seizures, slurred speech, confusion, or increased urination. Patients should seek immediate medical attention if these symptoms arise. Patients should not use diuretics while taking lithium.

Other side effects of lithium include acne, weight gain, and excessive thirst. Patients should be reminded to drink 8-12 glasses of water or other fluids each day, maintain a regular diet, and not change the amount of salt in their diet unless this has been prescribed by their physician. Dehydration or excessive water consumption can affect one's lithium level, which can either concentrate or dilute the blood level. Providers may also monitor kidney function more frequently in people taking lithium as it can have a detrimental effect on the kidneys.

Carbamazepine also requires blood monitoring at the beginning of treatment and when the dosage is changed. The most common side

[11] *extended release formulations*: Medications that have been made so that they act over a long period of time and do not have to be taken as often; may be referred to as CR (controlled release) or XR / XL (extended release).

[12] *lithium toxicity*: The quality, state, or relative degree of being poisonous, in this instance because of the presence or concentration of too much of the medication lithium in the blood.

effects include nausea, dizziness, and sedation. It can also cause more serious blood dyscrasias and skin rash.

Valproic acid levels will be taken just after initiation of treatment and periodically when doses are changed. The most common side effects of valproic acid include weight gain, sedation and upset stomach. Providers may choose to monitor liver function more closely when using this medication. The use of valproic acid is contraindicated in those with liver impairment.

POTENTIAL SIDE EFFECTS

Common side effects of this class of medications include sedation and weight gain. Other potential side effects of antimanic medications/mood stabilizers include:

- Blurred vision
- Coma*
- Diarrhea*
- Drowsiness
- Hand tremor*
- Increased thirst and urination*
- Inflammation of the pancreas
- Irregular heartbeats
- Kidney damage*
- Liver inflammation, hepatitis
- Nausea or vomiting
- Problems with the blood, both red and white cells
- Rash and skin changes
- Seizures
- Under or overactive thyroid*
- Weakness

*These side effects are associated with lithium, anticonvulsants, and atypical antipsychotics only. Effects vary greatly between persons.

EMERGENCY CONDITIONS

Lithium overdose is a life-threatening emergency. Signs of lithium toxicity may include nausea, vomiting, diarrhea, drowsiness, mental dullness, slurred speech, confusion, dizziness, muscle twitching, irregular heartbeat and blurred vision. An overdose of any of the other antimanic medications is always considered an emergency and treatment should be sought immediately.

Stevens-Johnson syndrome is a rare, serious disorder in which skin and mucous membranes react severely to a medication or infection. It can develop in those taking anticonvulsant medications. It typically starts with flu-like symptoms and progresses to painful red or purplish rash that spreads and blisters, eventually causing the top layer of the skin to die and shed. It is considered a medical emergency and requires hospitalization. Recovery can be extended, from weeks to months, depending on the severity of the condition. It has been especially noted with the use of lamotrigine (**Lamictal**). Any rash that develops while taking anticonvulsant medications should be promptly reported.

POTENTIAL FOR ABUSE OR DEPENDENCE

Abuse of antimanic/mood-stabilizing medications is considered uncommon. There are case reports in the literature that do however show the potential for abuse of lithium. The abuse potential comes from the fact that lithium can produce a “buzz” at high doses. This can be quite dangerous as lithium intoxication can occur with standard treatment doses of lithium and certain food, drink and drug interactions.

Anticonvulsant medications are also used in the treatment of mania. Their abuse potential alone is low; however, combining anticonvulsants with alcohol on the other hand can lead to increased drowsiness. Physical dependence has not been associated with lithium or anticonvulsants to date. Patients that are on lithium may experience manic episodes if it is stopped without a taper period. Patients on anticonvulsants should not stop their medica-

tions without medical supervision. Abrupt discontinuation of anticonvulsants may result in seizures. Slow tapering off periods (two to four weeks depending on the medication) are recommended to slow or prevent the withdrawal effects described. For patients with active seizures after sudden withdrawal of anticonvulsants, benzodiazepines like diazepam and lorazepam may be used to treat the immediate seizure.

CAUTIONS

- Doctors and pharmacists should be told about all medications being taken and dosage, including over-the-counter preparations, vitamins, minerals, and herbal supplements (such as St. John's wort, echinacea, ginkgo, ginseng, etc.).
- People taking mood-stabilizing medications should not increase their dose unless this has been checked with their physician and a change is ordered.
- Persons taking mood-stabilizing medications are particularly vulnerable to adverse medical consequences if they concurrently use alcohol and/or street drugs.
- Lithium can cause cardiac anomalies in infants exposed to lithium in utero during the first three months of pregnancy.
- Thyroid function must be monitored if a person takes lithium.
- Heavy sweating or use of products that cause excessive urination (for example, coffee, tea, some high caffeine sodas, use of diuretics, etc.) can lower the level of lithium in the blood.
- Blood tests for medication levels need to be checked every one to two months.
- Use of these medications will lower the effectiveness of birth control medications.

SPECIAL CONSIDERATIONS FOR PREGNANT WOMEN

Lithium exposure in pregnancy may be associated with a small increase in congenital cardiac malformations (Ebstein's anomaly) (Stahl, 2011). Those exposed to lithium before week 12 of gestation are at increased risk of heart abnormalities. For women taking lithium, blood levels of the medication should be monitored every two weeks. Ultrasound examinations should be performed on the fetus to rule out the development of an enlarged thyroid (goiter) in the unborn child (Mortola, 1989).

Carbamazepine exposure in pregnancy is associated with fetal carbamazepine syndrome. It should be avoided in pregnancy, if possible, especially during the first trimester (ACOG, 2009).

Exposure to valproate during pregnancy has been associated with an increased risk of fetal anomalies, including neural tube defects, fetal valproate syndrome, and long-term adverse neurocognitive effects. It should be avoided in pregnancy, if possible, especially during the first trimester (ACOG, 2009).

Generally, the use of mood-stabilizing antipsychotic medications should be avoided in the first trimester unless the mother poses a danger to herself, to others, or to the unborn child, or if the mother shows signs of profound psychosis (Cohen, 1989). Tapering and discontinuation of antipsychotic medication 10 days to two weeks before delivery is generally advised, though the way this is done varies by medication (Mortola, 1989).

For women of childbearing age who may be or think they may be pregnant, the physician should discuss the safety of these medications before starting, continuing, or discontinuing medication treatment. Practitioners may have a role in encouraging this discussion by suggesting their clients talk with the prescribing physician.

Antidepressant Medications

GENERIC	BRAND
SSRIs — Selective Serotonin Reuptake Inhibitors	
citalopram	Celexa
escitalopram	Lexapro
fluoxetine	Prozac, Prozac Weekly, Sarafem
fluvoxamine	Luvox
paroxetine	Paxil, Paxil CR
sertraline	Zoloft
vilazodone	Viibryd
SNRIs — Serotonin Norepinephrine Reuptake Inhibitors	
desvenlafaxine	Pristiq
duloxetine	Cymbalta
levomilnacipran	Fetzima
venlafaxine	Effexor, Effexor ER
Other antidepressants	
bupropion	Wellbutrin, Wellbutrin SR, Wellbutrin XL
mirtazapine	Remeron, Remeron SolTab
trazodone	Desyrel
Tricyclics & quatracyclics	
amitriptyline	Elavil
amoxapine	Asendin
clomipramine	Anafranil
desipramine	Nopramin
doxepin	Sinequan
imipramine	Tofranil
maprotiline	Ludiomil
nortriptyline	Aventyl, Pamelor
protriptyline	Vivactil
trimipramine	Surmontil
Monoamine Oxidase (MAO) Inhibitors	
isocarboxazid	Marplan
phenelzine	Nardil
selegiline transdermal patch	EMSAM
tranylcypromine	Parnate

PURPOSE

Antidepressant medications are used to treat a variety of mental health conditions including depression, bipolar illness, and anxiety disorders. Most antidepressants must be taken for a period of 3 to 4 weeks to begin to reduce or take away the symptoms of depression but a full therapeutic effect may not be present for several months.

SSRIs and SNRIs are considered first line medications for anxiety disorders such as generalized anxiety disorder (GAD), panic, and social anxiety disorder (SAD). SSRIs and SNRIs are also prescribed in higher doses to treat obsessive-compulsive disorders (Farach et al., 2012).

Positive early treatment responses to antidepressant medications include improved energy, concentration, and sleep. Later positive treatment responses include improved mood, attitude, and statements of "feeling better."

Treatment for a single episode of major depression should be continued for two years before discontinuing. Since major depression is a chronic recurrent illness for many people, long-term use of antidepressants is often indicated (much as one would take medication for high blood pressure or diabetes for a long period of time). Discontinuing antidepressant therapy before the depression is completely resolved may result in the person decompensating[13] and possibly becoming medication resistant. Untreated depression may result in suicide, especially with co-occurring

[13] *decompensate*: Loss of the body's ability to correct a defect by overdevelopment of or increased functioning of another organ or unimpaired parts of the same organ.

substance use disorders. Therefore, treatment for depression must be taken as seriously as treatment for any other major life-threatening illness.

TYPES OF ANTIDEPRESSANTS

SSRIs are the most frequently prescribed class of antidepressants because of their broad effectiveness, low side effects, and safety profile. They are thought to affect the serotonin[14] system to reduce symptoms of depression. The extended release formula of fluoxetine (**Prozac Weekly**) can be dosed once per week. **Sarafem** is fluoxetine under another label used for treatment of Premenstrual Dysphoric Disorder (PMDD). SSRIs include both less expensive generic medications (citalopram, fluoxetine, fluvoxamine, paroxetine, sertraline) and more expensive brand name only versions (escitalopram).

SNRIs (serotonin norepinephrine reuptake inhibitors) such as venlafaxine and desvenlafaxine work on both the serotonin and norepinephrine[15] levels.

Bupropion is an NDRI (norepinephrine dopamine reuptake inhibitor) that affects norepinephrine and dopamine levels in the brain. In addition, bupropion can be "activating" (as opposed to sedating) and is typically not used in those with anxiety disorders. It is not associated with weight gain or sexual dysfunction like many other antidepressant medications. Bupropion should be avoided by people who are at risk for or who currently have a seizure disorder since it can increase the possibility of having a seizure.

The MAO inhibitors and the tricyclic and quatracyclic antidepressants (named for their chemical structures) are older and less commonly used due to safety and side effects. MAOs are used for "atypical depressions," which produce symptoms like oversleeping, anxiety or panic attacks, and phobias. Also, they may be used when a person does not respond to other antidepressants. The older tricyclics may be preferred in spite of their common side effects because they are inexpensive. MAO inhibitors should not be stopped without medical supervision. MAO inhibitors have many medication and food interactions that can last up to 14 days after stopping them.

USUAL DOSE, FREQUENCY & SIDE EFFECTS

All medications have specific doses and frequencies. The physician will specify the exact amount of medication and when it should be taken. This information is provided on the prescription bottle. Several factors are considered before an antidepressant is prescribed: the type of medication, the person's individual body chemistry, weight, and age. Generally, people are started on a low dose, and the dosage is slowly raised until the optimal effects are reached without troublesome side effects.

Both mild sedation and mild agitation sometimes occur with SSRI use. The most troubling SSRI side effect is decreased sexual performance, which may be difficult for many persons to discuss. Common side effects specific to both bupropion and venlafaxine include sleeplessness and agitation. For the older tricyclics, side effects include dry mouth and sedation.

POTENTIAL SIDE EFFECTS

SSRIs

- Anxiety, agitation or nervousness
- Change in appetite (lack of or increase)
- Change in sexual desire
- Confusion
- Decrease in sexual ability
- Diarrhea or loose stools

[14] *serotonin*: A type of neurotransmitter in the brain.
[15] *norepinephrine*: A hormone secreted by the adrenal gland, which (together with epinephrine) brings about changes in the body known as the "fight or flight" reaction. It works as a neurotransmitter in the brain.

- Dizziness
- Dry mouth
- Headache
- Heart rhythm changes
- Increased sweating
- Insomnia or sleepiness
- Lack or increase of appetite
- Shakiness
- Stomach upset
- Taste disturbances (bupropion)
- Weight loss or gain

Tricyclics & quatracyclics

- Allergic reactions
- Blood cell problems (both white and red cells)
- Blurred vision
- Change in sexual desire
- Changes in heartbeat and rhythm
- Constipation
- Decrease in sexual ability
- Difficulty with urination
- Dizziness when changing position
- Dry mouth
- Fatigue
- Heart block[16]
- Increased sweating
- Kidney failure (amoxapine)
- Muscle twitches
- Neuroleptic Malignant Syndrome (amoxapine)
- Seizures (bupropion)
- Stroke
- Weakness
- Weight gain

MAO Inhibitors

- Blood cell problems (both white and red cells)
- Dizziness when changing position
- Fluid retention (swollen ankles, feet, legs or hands)
- Headache
- High blood pressure crisis[17]
- Insomnia
- Lack of appetite
- Rapid heartbeat

EMERGENCY CONDITIONS

Serotonin syndrome results from elevated levels of serotonin, usually due to concomitant use of two or more antidepressants (MAOIs, SSRIs) that interfere with serotonin levels in the brain. Symptoms are quite varied and can include headache, agitation, confusion, hallucinations; sweating, fever, shivering, tremors, muscle rigidity, uncontrollable posturing, seizures, and coma; abdominal pain, diarrhea, flushing, hypertension, enlarged pupils, salivation, rapid breathing and rapid heartbeat. Hyperthermia is common. The syndrome is potentially fatal and is treated symptomatically by removing the offending drugs and giving intravenous rehydration (Boyer, & Shannon, 2005; Wimbiscus, Kostenki, & Malone, 2010).

Food and beverage interactions. MAOIs can cause dangerous interactions with foods and beverages that contain high levels of tyramine —an amino acid that regulates blood pressure. The following foods contain tyramine and should be avoided when taking MAOIs:

aged cheeses and meats

banana peel

concentrated yeast extracts (Marmite)

draft beer (including alcohol-free beer)

[16] *heart block:* A condition where the heart beats irregularly or much more slowly than normal. Sometimes the heart may even stop for up to 20 seconds; caused by a delay or disruption of the electrical signals that usually control the heartbeat.

[17] *high blood pressure crisis*: A severe increase in blood pressure that can lead to stroke. Two types–emergency and urgent–require immediate medical attention.

fava beans
broad bean pods
smoked or aged meat, fish, or poultry
sauerkraut, kimchee
soybean products
tyramine-containing nutritional supplements

Consuming these foods while taking MAOIs can cause a hypertensive crisis and is considered a medical emergency (Wimbiscus et al., 2010).

An overdose of any of the MAO inhibitors, tricyclics, quatracyclics, or other antidepressants is serious and potentially life threatening and *must be reported to a physician immediately*. Symptoms of tricyclic and quatracyclic overdose may include rapid heartbeat, dilated pupils, flushed face, agitation, loss of consciousness, seizures, irregular heart rhythm, heart and breathing stopping, and death.

The potential for a fatal outcome from an overdose with the SSRIs is much less. However, the possibility that a person has attempted suicide should be dealt with as an emergency situation that needs immediate intervention.

POTENTIAL FOR ABUSE OR DEPENDENCE

A review conducted in 1998 determined that based on diagnostic end points, antidepressants as a class are not drugs of abuse (Lichtigfeld & Gillman, 1998). Nor do the agents cause physical dependence. However, withdrawal reactions have been reported with both the traditional (tricyclic and tetracyclic agents) and the novel (selective serotonin and norepinephrine reuptake inhibitors) antidepressants. Withdrawal symptoms of all the antidepressants can include: insomnia, anxiety, dizziness, upset stomach and headache. MAO inhibitor withdrawal can cause these symptoms in addition to muscle twitches, aggression, hallucinations and delirium. Slow gradual tapering off for all the antidepressants is recommended. While there is no defined taper schedule, tricyclic agents and MAO inhibitors should be tapered gradually over one to three months. For management of the tricyclic antidepressant withdrawal, benztropine has been used with some success (Warner, Bobo, Warner, Reid & Rachal, 2006).

CAUTIONS

- Doctors and pharmacists should be told about all medications being taken and dosage, including over-the-counter preparations, vitamins, minerals, and herbal supplements (such as St. John's wort, echinacea, ginkgo, ginseng, etc.).
- People taking antidepressant medications should not increase their dose unless this has been checked with their physician and a change is ordered.
- Withdrawal from SSRIs and other new antidepressants can cause flu-like symptoms. Discontinuing antidepressant therapy should be done gradually under a physician's care.
- Several prescription and over-the-counter medications interact with MAOIs. It is largely for this reason that they are rarely used. Other medications should not be taken unless the treating physician approves them. Even a simple over-the-counter cold medication can cause life-threatening side effects. A waiting period of at least two weeks is necessary after you stop taking MAOIs and start another antidepressant. Common nonprescription medicines, particularly certain cold remedies and diet pills, can also be dangerous when taken with an MAOI. The following list of medications have been shown to have drug interactions with MAOIs:

  Amphetamines
  Bupropion (**Wellbutrin**)

Cyclobenzaprine (Flexeril)
Dextromethorphan (contained in many cough-and-cold remedies)
Linezolid (Zyvox)
Meperidine (**Demerol**)
Methadone
Mirtazapine (**Remeron**)
Other MAO inhibitors
Pentazocine (**Talwin**)
Propoxyphene (**Darvon**)
Selective serotonin reuptake inhibitors
Serotonin-norepinephrine reuptake inhibitors
Noncutaneous sumatriptans
Tricyclic antidepressants
Tramadol (**Ultram**)
St. John's wort

Weight-reducing preparations that contain vasoconstrictors (such as, pseudoephedrine, phenylephrine, phenylpropanolamine, ephedrine, etc.)

- People using MAO inhibitors should check all new medications with a physician or pharmacist before taking them.
- People taking antidepressant medications are particularly vulnerable to adverse medical consequences if they concurrently use alcohol and/or street drugs.
- If there is little to no change in symptoms after 3 to 4 weeks, talk to the doctor about raising the dose or changing the antidepressant.
- Treatment with antidepressants usually lasts a minimum of 9 to 12 months. Many patients are on long-term antidepressant therapy to avoid the frequency and severity of depressive episodes.

Black Box warnings exist on many SSRIs as they have been deemed by the FDA to increase the risk of suicidal ideation in children, adolescents and young adults.

SPECIAL CONSIDERATIONS FOR PREGNANT WOMEN

Using SSRIs is safer for the mother and fetus than using tricyclic antidepressants. Fluoxetine is the most studied SSRI in pregnancy and no increased incidence in birth defects has been noted, nor were developmental abnormalities of the nervous system observed in preschool-age children. However, possible withdrawal signs have been observed in the newborn. Fluoxetine is the recommended SSRI for use during pregnancy (Garbis & McElhatton, 2001, pp. 182-191).

Paroxetine use in pregnant women and women planning pregnancy should be avoided. Fetal echocardiography should be considered for women who are exposed to paroxetine in early pregnancy.

Treatment with all SSRIs or selective norepinephrine reuptake inhibitors or both during pregnancy should be individualized and weighed against the risks and benefits to the patient and the fetus.

MAO Inhibitor use is not advised in pregnancy, and its use should be discontinued immediately if a woman discovers she is pregnant (Mortola, 1989).

The physician should discuss the safety of antidepressant medications before starting, continuing, or discontinuing medication treatment with all women of childbearing age who may be or think they may be pregnant. Practitioners may have a role in encouraging this discussion between their clients and the prescribing physician.

Antianxiety Medications

GENERIC	BRAND
See also SSRI Antidepressants (p. 17)	
Benzodiazepines	
alprazolam	Xanax, Xanax XR, Niravam
chlordiazepoxide	Librium
clonazepam	Klonopin, Klonopin Wafers
clorazepate	Tranxene
diazepam	Valium
lorazepam	Ativan
oxazepam	Serax
Beta-blockers	
propranolol	Inderal
Other	
buspirone	BuSpar
gabapentin*	Neurontin*
hydroxyzine*	Atarax*, Vistaril*
pregabalin*	Lyrica*
tiagabine*	Gabitril*

*Use of these medications for the treatment of anxiety disorders is "off label."

PURPOSE

Antianxiety medications are used in many psychiatric conditions including anxiety spectrum disorders, mood disorders, psychotic conditions, and for sleep. They enhance a sense of calm and can be used alone or in combination with other psychiatric medications.

Selective Serotonin Reuptake Inhibitors (SSRIs) are among the safest drugs used to treat anxiety disorders. They are typically first line treatment for anxiety spectrum disorders, which include generalized anxiety disorders (GAD), social anxiety disorders (SAD), post-traumatic stress disorders (PTSD), panic disorder and obsessive compulsive disorder (OCD). The safety, efficacy, and side effect profile of this class of drugs are one reason they are so widely used. In spite of this, black box warnings exist on many SSRIs as they have been deemed by the FDA to increase the risk of suicidal ideation in children, adolescents and young adults.

Other commonly used medications for the treatment of anxiety disorders include serotonin norepinephrine reuptake inhibitors (SNRIs), benzodiazepines, mood stabilizers, beta blockers and antipsychotics, although not all of these are FDA approved.

Positive treatment response to antidepressant medications (such as SSRIs and SNRIs) includes a gradual reduction in anxiety, panic, and PTSD or OCD symptoms over weeks to months.

Benzodiazepines have a calming effect by acting on gamma-aminobutyric acid (GABA)[18] receptors in the brain. Positive treatment response to benzodiazepines occurs rapidly from 30 to 60 minutes to a few hours for most antianxiety medications. For those with co-occurring substance use disorders, the response may be short-lived and tolerance develops leading to the need for increased doses. Combined with alcohol, there is a synergistic effect adding to the level of sedation one experiences. Physicians may use them for a short time as alcohol withdrawal medicines, or as sedatives in acute[19] psychotic or manic episodes. If used in outpatient settings, careful monitoring for tolerance and abuse

[18] *gamma aminobutyric acid (GABA)*: A type of neurotransmitter in the brain.

[19] *acute*: Having a sudden onset and short duration (*acute* disease). Urgent or critical condition.

is needed. Benzodiazepines are intended for short term use because of their abuse potential and the development of tolerance.

Beta-blockers work on the central nervous system to reduce the flight or fight response. Propranolol occasionally prescribed for performance anxiety, is not addictive.

Niravam (alprazolam) and **Klonopin wafers** (clonazepam) use an oral disintegrating tablet to make the active ingredients faster acting. By dissolving under the tongue, the medication will work much faster (within 15 minutes) than standard tablets that can take up to 30 minutes or longer to work.

Buspirone works through the serotonin system to induce calm. It is FDA approved for the management and short term treatment of anxiety disorders. It lacks the dependence and tolerance issues associated with benzodiazepines. It is deemed as the most effective in the treatment of GAD with associated depressive symptoms (Stahl, 2011, p.77; Egger & Hebert, 2011).

Hydroxyzine is an antihistamine that uses the drowsiness side effect of the antihistamine group to calm and relax. Hydroxyzine works within an hour of being taken. Buspirone and hydroxyzine do not lead to physical or psychological dependence or a substance use disorder.

Low doses of risperidone, quetiapine, olanzapine or other atypical antipsychotics are sometimes used "off label" as non-addictive antianxiety medications. They are usually used when several other medications have failed (though use of atypical antipsychotics is expensive and not FDA approved for treatment of anxiety disorders). Their special formulation works to reduce anxiety and help the person think more clearly, though the mechanism for this is unclear.

Gabapentin, tiagabine, and pregabalin have all been used to treat anxiety (off label) especially in those persons with a substance use disorder history and for whom antidepressants have been effective. These agents are all mildly sedative, and do not cause a high dependence, or withdrawal. They are thought to enhance the effects of the body's own naturally produced calmative agent by blocking excitatory neurons on the brain. Although none of these medications are FDA approved for treatment of anxiety disorders.

USUAL DOSE, FREQUENCY & SIDE EFFECTS

All medications have specific doses and frequencies. The physician will specify the exact amount of medication and when it should be taken. This information is provided on the prescription bottle. People are sometimes started on a low dose of medication, which is raised gradually until symptoms are removed or diminished (however, this is not always the case, as it depends on the illness and severity). Major factors considered in establishing the correct dose are individual body chemistry, weight, and ability to tolerate the medication.

People taking benzodiazepines for longer than 4 to 8 weeks may develop physical tolerance to the medication. This is especially true in those with a history of substance use disorder. Even when taken as directed, withdrawal symptoms may occur if regular use of benzodiazepines is abruptly stopped. Withdrawal from high dose use of benzodiazepines may be a life-threatening situation. For these reasons benzodiazepines are usually prescribed for brief periods of time—days or weeks—and sometimes intermittently for stressful situations or anxiety attacks. Discontinuation of benzodiazepines should be done under the direction of your provider, who will develop a tapering schedule to safely decrease your dose over a period of time. Except for treating alcohol or benzodiazepine withdrawal, or for acute sedation in manic or psychotic states, benzodiazepines are not recommended for

most people with a past or current history of substance use disorder or dependence (Lader, 2011).

Beta-blockers act on the sympathetic nervous system and are not considered addictive. They also are used to treat high blood pressure, thus side effects might be low blood pressure or dizziness. Beta-blockers may enhance the effects of other psychotropic medications and are inexpensive. Propranolol is taken as needed for performance anxiety. It is taken on a regularly scheduled basis for treatment of high blood pressure and other heart conditions.

Buspirone (not to be confused with bupropion) is often used to control GAD and is considered safe for long-term therapy.

Hydroxyzine is a safe and non-habit forming medication used to reduce anxiety. It is inexpensive and may be used for longer-term therapy. Because it is an antihistamine, common side effects are dry mouth and sedation. A less common side effect is urinary retention in older men; this is a serious condition.

POTENTIAL SIDE EFFECTS

Potential side effects vary by drug class. (See side effects of SSRIs, SNRIs under antidepressant medications.)

Benzodiazepines

Common side effects of benzodiazepines include drowsiness, dependence and tolerance, psychomotor impairment, memory impairment, confusion, dizziness, and mood changes.

Other potential side effects

- Blood cell irregularities
- Constipation
- Depression
- Drowsiness or lightheadedness
- Dry mouth
- Fatigue
- Heart collapse (weakened heart muscles)
- Loss of coordination
- Memory impairment (propranolol)
- Mental slowing or confusion
- Slowed heartbeat (diazepam)
- Stomach upset
- Suppressed breathing (restrained or inhibited)
- Weight gain

POTENTIAL FOR ABUSE OR DEPENDENCE

In the United States, the misuse and abuse of benzodiazepines are widespread. The most frequently abused benzodiazepines are alprazolam, clonazepam, lorazepam and diazepam (Substance Abuse and Mental Health Services Administration SAMHSA, 2006).

Between 11 and 15% of people in the U.S. take a form of antianxiety medication—including benzodiazepines—at least once each year. If antidepressants are included, this figure is doubled. Benzodiazepines may cause at least mild physical dependence in almost everyone who uses the medication for longer than six months (for example, if the medicine is abruptly stopped, the person will experience anxiety, increased blood pressure, fast heartbeat, and insomnia). However, becoming physically dependent on benzodiazepines does not necessarily mean a person will become psychologically dependent or addicted to the medication. Most people can be gradually withdrawn from the medication—when indicated—and will not develop psychological dependence. Benzodiazepines have a relatively low potential for abuse in those without substance use disorder histories, but moderate or higher potential in those with substance use disorder histories.

In general, abuse and dependence occur at lower rates with long-acting antianxiety medications (e.g., clonazepam, oxazepam

and clorazepate). Abuse and dependence are more likely to occur with faster-acting, high-potency antianxiety medications (such as alprazolam and lorazepam).

Risk Factors Related to Developing Dependency on Antianxiety Medication:

Less than 1% of persons who do not have a current substance use disorder or a history of substance use disorder becomes dependent on antianxiety medications. These people are at ***little or no risk***. They are more likely to skip doses, take lower doses than prescribed, or decrease their dose over time.

People with a prior history of substance use disorder or dependence who are in recovery are at increased risk of becoming dependent on antianxiety medications. These people are at ***moderate risk***.

Those with a history of abusing antianxiety medications or those who are opiate users are at ***higher risk*** of becoming dependent on antianxiety medications. Some studies indicate there is a moderately higher risk for persons who are dependent on alcohol to become dependent on antianxiety medications.

EMERGENCY CONDITIONS

Benzodiazepines do not cause respiratory depression (slower than normal breathing). When these medications are combined with other sedative medications (phenobarbital or opioids) or combined with alcohol, the sedation is much greater. Under these conditions respiratory depression, which is a life-threatening medical emergency, can occur. Overdose on the older tricyclic antidepressant medications, which are often used for combined anxiety depression disorders, can be life threatening and immediate referral to emergency care is indicated.

Withdrawal from regular use of any of the benzodiazepines and similar medications must be done slowly over a month's time. Abrupt withdrawal from these medications can cause hallucinations, delusions and delirium, disorientation, difficulty breathing, hyperactivity, and grand mal seizures. A protocol for decreasing or tapering off doses of benzodiazepines is needed.

CAUTIONS

- Doctors and pharmacists should be told about all medications being taken and dosage, including over-the-counter preparations, vitamins, minerals, and herbal supplements (such as St. John's wort, echinacea, ginkgo, ginseng, etc.).
- People taking antianxiety medications should not increase their dose unless this has been checked with their physician and a change is ordered.
- People should not stop using these medications without talking to a doctor.
- People taking antianxiety medication are particularly vulnerable to adverse medical consequences if they concurrently use alcohol and/or street drugs.
- Using alcohol in combination with benzodiazepines may result in breathing failure and sudden death.
- Propranolol occasionally prescribed for performance anxiety, will lower your pulse (heart rate) and can lead to fatigue (tired feeling) with continued use. Certain medications and medical conditions can be impacted by propranolol. Be sure to keep the doctor and pharmacists aware of all medications and medical conditions a client may have.

SPECIAL CONSIDERATIONS FOR PREGNANT WOMEN

The current state of knowledge suggests that benzodiazepine therapy in general does not pose as much risk of producing a baby with deformations as compared to anticonvulsants

(for example, valproic acid) as long as they are given over a short time period. It appears that short-acting benzodiazepines, like those used to treat alcohol withdrawal (detoxification[20]), can be used in low doses even in the first trimester (Robert et al., 2001). Long-acting benzodiazepines should be avoided—their use during the third trimester or near delivery can result in a withdrawal syndrome in the baby (Garbis & McElhatton, 2001). Furthermore, exposure to benzodiazepines shortly before delivery was found to be associated with floppy infant syndrome (ACOG, 2009). Additionally, a small risk was associated with prenatal benzodiazepine exposure, which increased the risk of oral cleft (absolute risk increased by 0.01%) (ACOG, 2009).

For use of the SSRIs in pregnancy, see page 21.

During pregnancy, the capacity of many drugs to bind to proteins[21] is decreased, including diazepam (a benzodiazepine) and methadone (Adams & Wacher, 1968; Dean et al., 1980; Ganrot, 1972) with the greatest decrease noted during the third trimester (Perucca & Crema, 1982). From a clinical standpoint, pregnant women could be at risk for developing greater toxicity[22] and side effects to these medications. Yet at the same time, increased metabolism of the medication may result, reducing the therapeutic effect (such as with methadone since many women seem to require an increase in their dose of methadone during the last trimester) (Pond et al., 1985). In addition, there is a documented withdrawal syndrome in newborns exposed to benzodiazepines in utero (Sutton & Hinderliter, 1990). Onset of this syndrome may be delayed more so than that associated with other drugs.

For all women of childbearing age who may be or think they may be pregnant, the physician should discuss the safety of this medication before starting, continuing, or discontinuing medication treatment. Practitioners may have a role in encouraging this discussion by suggesting their clients talk with the prescribing physician.

[20] *detoxification*: A medical and biopsychosocial procedure that assists a person who is dependent on one or more substance to withdraw from dependence on all substances of abuse.

[21] *protein binding*: The affinity of a drug to attach (*bind*) to blood plasma proteins. The extent to which a drug is *bound* to plasma can affect the distribution of the drug in the body. In most cases, binding to plasma proteins is reversible.

[22] *toxicity*: Poisonous nature; poisonous quality.

Stimulant Medications

GENERIC	BRAND
armodafinil	Nuvigil
d-amphetamine*	Dexedrine*, Dextrostat*
dexmethylphenidate	Focalin
l & d-amphetamine*	Adderall*, Adderall XR*
methamphetamine	Desoxyn
methylphenidate*	Ritalin*, Ritalin SR*, Ritalin LA*, Concerta*, Metadate ER,* Metadate CD*, Methylin ER*, Daytrana*, Quillivant XR*
modafinil	Provigil
lisdexamfetamine *	Vyvanse*

Non-stimulants for ADHD[23]

atomoxetine*	Strattera*
bupropion	Wellbutrin, Wellbutrin SR, Wellbutrin XL
guanfacine*	Tenex*, Intuniv*

**FDA approved for treatment of ADHD*

PURPOSE

Stimulant medications are used most often to treat attention deficit/hyperactivity disorder (ADHD), which is typically diagnosed in childhood but also occurs in adults. They are also used in narcolepsy[24], and off label for treatment resistant depression, and lethargy/psychomotor retardation associated with some medical conditions. Symptoms consistent with ADHD include short attention span, excessive activity (hyperactivity), impulsivity, and emotional development below the level expected for the person's age. The underlying manifestation of ADHD is that it severely impacts and interferes with a person's daily functioning.

Positive treatment responses to stimulant medications include increased attention, focus and/or ability to stay on task, less hyperactivity, and moderation of impulsive behavior. People with ADHD generally report that they feel "normal" when taking stimulants.

Non-stimulant medications for ADHD differ somewhat. Atomoxetine blocks the reuptake of norepinephrine, which helps reduce the symptoms of ADHD. Guanfacine and bupropion are non-stimulants that have been used successfully to treat symptoms of ADHD. The advantage of these medications is that they are non-addictive, and do not cause a "high" even in larger doses. Atomoxetine is FDA approved. While studies have shown bupropion to be effective, it is not FDA approved.

USUAL DOSE & FREQUENCY

All medications have specific doses and frequencies. The physician will specify the exact amount of medication and when it should be taken. This information is provided on the prescription bottle. With stimulants, there may be periods when the medication is not to be taken. The most common side effects of the stimulants are nervousness, sleeplessness, and loss of appetite. Some of these medications are expensive, but others are generic and quite inexpensive.

POTENTIAL SIDE EFFECTS

Stimulants

- Blood disorders (methylphenidate)
- Anxiety/agitation
- Change in heart rhythm
- Delayed growth

[23] *ADHD*: Refers to two types of disorders. Attention deficit disorder without hyperactivity (**ADD**), and attention deficit disorder with hyperactivity (**ADHD**). The terms are often used interchangeably.

[24] *narcolepsy*: A condition characterized by brief attacks of deep sleep.

- Dilated pupils
- Elevated blood pressure
- Euphoria
- Excitability
- Increased pulse rate
- Insomnia
- Irritability
- Loss of appetite
- Mood swings
- Rash
- Seizures (methylphenidate)
- Tremor

Non-stimulants for ADHD

Atomoxetine side effects include:

- Constipation
- Dry mouth
- Nausea
- Fatigue
- Decreased appetite
- Insomnia
- Erectile dysfunction
- Urinary hesitation and/or urinary retention and/or dysuria
- Dysmenorrhea
- Hot flush
- Rare skin rashes
- High blood pressure
- Nervousness, and side effects similar to some antidepressants

Bupropion side effects include:

- Increased chance of seizure activity
- Dry mouth
- Constipation
- Loss of appetite
- Insomnia
- Dizziness
- Sweating
- Rash
- Hypertension

Guanfacine side effects include:

- Constipation
- Dizziness
- Dry mouth
- Low blood pressure
- Sleepiness

POTENTIAL FOR ABUSE OR DEPENDENCE

Stimulant medications are among the most commonly abused psychiatric medications and have the potential for misuse by those taking them for treatment. Recreational or non-medically indicated uses have been reported for performance enhancement and/or weight loss. People with ADHD or narcolepsy, however, rarely abuse or become dependent on stimulant medications unless they have other substance use problems.

Most doctors use antidepressants or atomoxetine (both non-stimulants) to treat ADHD in adults with co-occurring substance use disorders. Using stimulant medications to treat ADHD in children has been shown to reduce the potential development of substance use disorders.

EMERGENCY CONDITIONS

Psychiatric symptoms including paranoid delusions, thought disorders, and hallucinations have been reported when stimulants are used for long periods or taken at high dosages. Overdose with stimulants is a medical emergency. Seek help immediately.

CAUTIONS

- Doctors and pharmacists should be told about all medications being taken and dosage, including over-the-counter preparations, vitamins, minerals, and herbal supplements (such as St. John's wort, echinacea, ginkgo, ginseng, etc.).
- People taking stimulant medications should not increase their dose unless this has been checked with their physician and a change is ordered.

- People taking stimulant medications are particularly vulnerable to adverse medical consequences if they concurrently use alcohol and/or street drugs.
- With stimulants, there is the potential for development of tolerance and dependence on the medications with accompanying withdrawal. The potential for abuse and misuse is high, as is true with all Schedule II drugs[25].

Patients who have heart disease or cardiac abnormalities, hypertension or hypotension, or liver disease should not use atomoxetine.

SPECIAL CONSIDERATIONS FOR PREGNANT WOMEN

For women of childbearing age who may be or think they may be pregnant, the physician should discuss the safety of this medication before starting, continuing, or discontinuing medication treatment. Practitioners may have a role in encouraging this discussion by suggesting their clients talk with the prescribing physician. Risks versus benefits should be weighed against the potential harm to the unborn fetus.

[25] *Schedule II drugs*: Drugs classified in *Schedule II* of the Controlled Substances Act; have a high potential for abuse with severe liability to cause psychic or physical dependence, but have some approved medical use.

Narcotic and Opioid Analgesics

Natural opioids

Opium, morphine and codeine products

Pure, semi or totally synthetic derivatives

Hydrocodone, methadone, oxycodone and others

GENERIC	BRAND
buprenorphine	Butrans, Subutex
butorphanol	Stadol nasal spray
codeine	Codeine
fentanyl	Duragesic, Fentora, Actiq, Onsolis, Ionsys
hydromorphone	Dilaudid, Exalgo
levorphanol	Levo-Dromoran
meperidine	Demerol
methadone	Dolophine, Methadose
morphine	Kadian, MS Contin, MS IR, Oramorph, Roxanol
oxycodone	Roxicodone, Oxycontin, Oxyfast
oxymorphone	Opana, Opana ER
pentazocine	Talwin
propoxyphene	Darvon
tramadol	Ultram

The following products use a combination of an opioid or narcotic along with aspirin, acetaminophen, or other pain reliever to treat mild to moderate pain.

Anexsia 5/500

Capital with Codeine

E-Lor or Wygesic

Empirin or Phenaphen with Codeine #3

Empirin or Phenaphen with Codeine #4

Endocet

Fioricet with Codeine

Fiorinal with Codeine

Lorcet Plus

Lortab

Maxidone

Percocet

Percodan

Roxicet

Roxicet oral solution (contains alcohol)

Roxiprin

Talacen

Talwin Compound

Tylenol with Codeine

Tylenol with Codeine syrup (contains alcohol)

Tylox

Vicodin

Vicodin ES

Zydone

The following products use a combination of an opioid or narcotic along with an opioid antagonist which blocks the "high" that opioids can have if used inappropriately. They are designed to prevent abuse of the opioid but still provide pain relief when used as prescribed.

Acurox

Embeda

Oxytrex

Suboxone

PURPOSE

Opiate medications are commonly used to control moderate to severe acute pain. They are typically used for a short time because they cause physiological tolerance (takes more to get the same analgesic effect) and physical dependence (get withdrawal symptoms if abruptly stopped) as amount and duration of doses increase. Longer-term use is indicated to alleviate the chronic pain associated with cancer and certain other conditions, and research has shown that abuse of these medications rarely occurs in such patients. Severe and chronic pain has long been under treated in the United States due to irrational fears that anyone prescribed opiates will

become addicted. This has clearly been shown to be not the case. People with substance use disorders need pain management like anyone else. Opioids are appropriately prescribed to manage chronic cancer pain—especially fentanyl, oxycodone and methadone.

Opioid agonists, partial agonists, and antagonists are also used to treat addiction to opioid substances. Acute opioid-related disorders that require medical management include opioid intoxication, opioid overdose, and opioid withdrawal (see page 40 of this publication for more information on opioid use disorders treatment).

Methadone is a medication used in opioid detoxification treatment programs to maintain sobriety from opioid use disorders. Many people who have been addicted to heroin and other opioids have returned to a productive life because of methadone treatment (heroin is a drug of abuse). Methadone is also frequently used to provide relief for specific types of pain, especially in pain clinics. The management of chronic pain in persons with a history of opioid use disorders is one of the most challenging tasks in medicine.

USUAL DOSE & FREQUENCY

All narcotic and opioid analgesics have specific doses and frequencies. The physician will specify the exact amount of medication and when it should be taken. This information is provided on the prescription bottle. Many narcotic or opioid medications are taken two or more times a day. Some medications are taken in pill or liquid form. A few are taken in a nasal spray or as topical patches on the skin. Injectable narcotics are not listed here because they are not often used outside a hospital setting.

POTENTIAL SIDE EFFECTS

- Constipation
- Decreased ability to see clearly
- Decreased ability to think clearly
- Flushing and sweating
- Itching
- Pupil constriction
- Respiratory depression (slowed breathing rate)
- Stomach upset
- Tolerance

POTENTIAL FOR ABUSE OR DEPENDENCE

Opioids are among the three most commonly abused prescription drugs in the U.S. (the others being central nervous system depressants and stimulants).

With narcotic and opioid medications, there is a potential for the development of tolerance and dependence as well as the possibility of abuse and severe withdrawal reactions. There are many non-addictive pain medications available for pain management that can be used after acute pain is reduced.

EMERGENCY CONDITIONS

Convulsions and/or cardiac arrest with high dosages.

Overdose may increase pulse rate, result in convulsions followed by coma or death.

Overdose may depress the breathing centers in the brain leading to inability to breathe.

An overdose is always considered an emergency and treatment should be sought immediately.

CAUTIONS

- Doctors and pharmacists should be told about all medications being taken and dosage, including over-the-counter preparations, vitamins, minerals, and herbal supplements (such as St. John's wort, echinacea, ginkgo, ginseng, etc.).
- People taking narcotic and opioid analgesics should not increase their dose unless this

has been checked with their physician and a change is ordered.

- Because of the risk of respiratory depression, opioid narcotics should not be used in combination with alcohol, antihistamines, barbiturates, benzodiazepines, or general anesthetics.
- Persons taking an opioid medication are particularly vulnerable to adverse medical consequences if they concurrently use alcohol and/or street drugs, because alcohol and street drugs can increase the sedation effects of the opioids.
- Potential for development of tolerance and dependence exists.

SPECIAL CONSIDERATIONS FOR PREGNANT WOMEN

For all women of childbearing age who may be or think they may be pregnant, the physician should discuss the safety of this medication before starting, continuing, or discontinuing medication treatment. Both pregnant women and their unborn infants can become tolerant and physically dependent on opioids. This dependence as well as possible withdrawal syndromes needs to be assessed. Practitioners may have a role in encouraging this discussion by suggesting their clients talk with the prescribing physician. See p. 42 for information about methadone use during pregnancy.

Hypnotics (Sleep Aids)

GENERIC	BRAND
Barbiturates	
secobarbital	Seconal
Benzodiazepines	
estazolam*	ProSom*
flurazepam*	Dalmane*
quazepam*	Doral*
temazepam*	Restoril*
triazolam*	Halcion*
clonazepam	Klonopin
diazepam	Valium
lorazepam	Ativan
oxazepam	Serax
Non-benzodiazepines	
eszopiclone*	Lunesta*
ramelteon*	Rozerem*
zaleplon*	Sonata*
zolpidem*	Ambien*
diphenhydramine	Benadryl
Melatonin	
sedating antidepressants	Desyrel, Remeron, Serzone, Sinequan
sedating antipsychotics	Seroquel, Zyprexa, Zyprexa Zydis

**FDA approved for insomnia*

PURPOSE

Hypnotics are used to help people with sleep disturbances get restful sleep. Lack of sleep is one of the greatest problems faced by those with substance use disorders and is very common in those with psychiatric illnesses. It can exacerbate the symptoms of these disorders. For example, mood changes, psychosis and irritability increase with insomnia. Lack of sleep diminishes a person's ability to think clearly or process information. Sleep-wake cycles and the body's ability to heal itself also suffer when a person is sleep deprived. Older hypnotics, like barbiturates, cause the body to slow down and "pass out" or sleep. However, they also have a tendency to disturb sleep cycles. For this reason, and because of their potential for abuse and dependence, barbiturates are now rarely used.

Benzodiazepines are frequently used as a short-term treatment for insomnia. However, due to the risk of tolerance, dependence and subsequent withdrawal symptoms they are ideally used for periods no greater than four weeks. Gradual tapering is used to avoid symptoms of withdrawal which include anxiety, depression, nausea/vomiting, and rebound insomnia; therefore, gradual tapering of the dose is recommended.

Non-benzodiazepines such as zolpidem and zaleplon affect one of the body's receptors for the natural calming agent, GABA. These medications are short acting and do not disturb sleep-staging cycles. Rebound insomnia is a side effect of both, however, if the medications are used for more than two weeks and then abruptly stopped. Ramelteon works with the melatonin[26] pathways in the brain to help you fall asleep. It is non-habit forming and can be taken long term for chronic insomnia.

Sedating antidepressants work by using their sleep producing side effects to induce sleep. They are not addictive but have the capacity to produce all the side effects of their class of antidepressant. Sedating antipsychotics use their calming and sedation side effects to induce sleep but have the capacity to produce all the side effects of atypical antipsychotics

[26] *melatonin*: A type of neurotransmitter in the brain.

and they are an expensive alternative. Anticonvulsants may be used for sedation when treating acute or prolonged withdrawal symptoms from alcohol.

Antihistamines such as diphenhydramine and hydroxyzine work through their naturally sedating properties to induce sleep.

Paradoxically, those with substance use disorders (SUDs) can become rapidly tolerant and dependent on the most commonly used hypnotics, which are the benzodiazepines and even one of the non-benzodiazepines—zolpidem. Tolerance can lead to decreasing effectiveness, escalating doses, and an even worse sleep disorder when the agent is withdrawn. For this reason, most doctors treating SUDs use sedating antidepressants, anticonvulsants, or sedating antihistamines if the sleep problem continues past acute withdrawal symptoms.

USUAL DOSE & FREQUENCY

All medications have specific doses and frequencies. The physician will specify the exact amount of medication and when it should be taken. This information is provided on the prescription bottle. All of these medications are generally used for limited periods (3 to 4 days for barbiturates or up to a month for others). All of these medications quickly develop tolerance and eventually the usual dose will no longer help the person sleep.

POTENTIAL SIDE EFFECTS

- Breathing difficulty (**Seconal**)
- Dizziness
- Drowsiness
- Hangover feeling or daytime sleepiness
- Headache
- Lethargy
- Weakness

POTENTIAL FOR ABUSE OR DEPENDENCE

With hypnotics, there is the potential for development of tolerance and dependence on the medications with accompanying withdrawal. The potential for abuse and misuse is high. There are many drawbacks to long-term use of hypnotics such as damaged sleep staging and substance use disorders. Even zolpidem and zaleplon if taken for longer than 7 to 14 days, can have a discontinuation rebound insomnia effect. Non-habit-forming medications are available to treat insomnia.

EMERGENCY CONDITIONS

Overdose with any of these medications can be life threatening. Seek help immediately.

Combinations of alcohol and barbiturates or alcohol and benzodiazepines can be deadly.

CAUTIONS

- Doctors and pharmacists should be told about all medications being taken and dosage, including over-the-counter preparations, vitamins, minerals, and herbal supplements (such as St. John's wort, echinacea, ginkgo, ginseng, etc.).
- People taking hypnotic medications should not increase their dose unless this has been checked with their physician and a change is ordered.
- People taking hypnotic medications are particularly vulnerable to adverse medical consequences if they concurrently use alcohol and/or street drugs.
- There is potential for development of tolerance and dependence with accompanying withdrawal. Potential for abuse and misuse is high.

SPECIAL CONSIDERATIONS FOR PREGNANT WOMEN

Barbiturate use during pregnancy has been studied to some extent, but the risk of taking this medication should be discussed with the patient (Robert et al., 2001). There also are reports of a withdrawal syndrome in newborns following prenatal exposure to some barbiturates (Kuhnz et al., 1988).

Diphenhydramine and hydroxyzine have sometimes been used to treat insomnia during pregnancy. Diphenhydramine has no proven risks of fetal malformations. There is no human data of hydroxyzine use in humans, though malformations have been seen in studies with mice and rats at high doses. Although there are no human studies with zolpidem describing its use during pregnancy, adverse effects were noted with high doses in animal studies. Trazodone has shown both fetal toxicity and abnormalities at high doses (Briggs, Freeman, & Yaffe, 2002). Benzodiazepine use during pregnancy has been associated with "floppy infant syndrome" shortly after delivery (ACOG, 2009).

For all women of childbearing age who may be or think they may be pregnant, the physician should discuss the safety of this medication before starting, continuing, or discontinuing medication treatment. Practitioners may have a role in encouraging this discussion by suggesting their clients talk with the prescribing physician.

Alcohol Use Disorders Treatment Medications

GENERIC	BRAND
Alcohol Withdrawal Agents	
benzodiazepines	Valium, Librium, and Ativan
(e .g ., diazepam, chlordiazepoxide, and lorazepam)	
anticonvulsants	Tegretol, Depakote, Neurontin
(e .g ., carbamazepine, divalproex sodium, gabapentin)	
Alcohol Relapse Prevention Agents	
disulfiram*	Antabuse*
naltrexone*	ReVia*
naltrexone extended-release injection*	Vivitrol*
acamprosate*	Campral*
topiramate	Topamax

**FDA approved for treatment of Alcohol Use Disorders (AUDs).*

Note: For more information on benzodiazepines and anticonvulsants see Antimanic Medications, Antianxiety Medications and Hypnotics sections in this publication.

PURPOSE

Medications involved in alcohol use disorders treatment include those used for acute alcohol withdrawal as well as a growing number used for alcohol relapse prevention. The acceptance of alcohol relapse prevention medications in the field is growing. It is anticipated that within the next few years, medications like naltrexone and acamprosate will be more widely used given the developing body of research which indicates that these medications work for the treatment of alcohol dependence.

Alcohol withdrawal: Symptoms of alcohol withdrawal typically present within 12 hours of discontinuing the ingestion of alcohol. Though usually only treated for 1 to 5 days, signs and symptoms of alcohol withdrawal may present in varying degrees for weeks or months. Signs and symptoms of alcohol withdrawal differ in severity but may include the following: nausea, vomiting, tremor, sweating, tachycardia, anxiety, agitation, hallucinations, craving alcohol, and delirium tremens. A common tool used to assess the level of severity of alcohol withdrawal is the revised Clinical Institute Withdrawal Assessment for Alcohol scale (CIWA-Ar) (Sullivan, Sykora, Schneiderman, Naranjo, & Sellers, 1989).

Benzodiazepines are by far the most commonly used medications for acute withdrawal. Benzodiazepines work through the potentiation of GABA receptors with the most common differences among them being their onset of action, duration of action, and half-life. Typically symptoms of alcohol withdrawal can be managed with benzodiazepines over the course of a week or less. When used for longer periods of time there are concerns of potential tolerance and dependence. Thiamine is also recommended for treatment to reduce the risk of neurological deficits related to alcohol ingestion.

Anticonvulsants such as carbamazepine, divalproex sodium, and gabapentin are more commonly used in Europe. The advantage in using these medications is that they can be prescribed for weeks and months versus only days. Propranolol, a beta-blocker, and clonidine, an alpha-2 agonist, are sometimes used in alcohol withdrawal treatment along with either benzodiazepines or anticonvulsants to decrease anxiety, heart rate, sweating, and blood pressure. Antipsychotics may be used if the person develops severe alcohol withdrawal with hallucinations.

Alcohol relapse prevention: The oldest medication used in alcohol relapse prevention is disulfiram. It has been used for over 50

years. Disulfiram blocks the breakdown of alcohol by inhibiting aldehyde dehydrogenase, resulting in toxic acetaldehyde[27] levels in the body. This in turn leads to severe nausea and vomiting. The use of disulfiram is an aversive therapy and is more effective when used in persons motivated to take it regularly, or in those that receive it in a "monitored" fashion 3 to 5 times per week. It works by causing the person to rethink a move to impulsive drinking knowing that with disulfiram present they will likely experience significant nausea, vomiting, and the sensation of heat, headache, and flushing.

Naltrexone was first developed as a selective μ-opioid receptor blocker and used in monitored treatment programs for opioid dependence. Many persons with opioid addiction, however, stopped taking it and returned to opioid use or they preferred methadone maintenance therapy. In spite of this, clinical observation of persons taking naltrexone showed that those who also used alcohol seemed to drink less and reported that alcohol use affected them less. Subsequent controlled clinical trials comparing use of naltrexone to placebo condition have shown its effectiveness over placebo to decrease alcohol craving and relapse potential. However, in less structured aftercare settings naltrexone is not considered as effective.

A long-acting injectable form of naltrexone is now available and provides an additional unique delivery method. Use of this once monthly treatment, especially in those persons who are less motivated about their recovery, has led to a reduction in days drinking; and when drinking does occur, they consume less alcohol. Thus, some consider naltrexone as a harm reduction medicine more than a complete abstinence treatment enhancer.

Naltrexone is nonpsychoactive[28] and as an opioid receptor blocker, it can interfere with the use of opioids for treatment of acute pain. For more information on naltrexone, see TIP 49*: Incorporating Alcohol Pharmacotherapies into Medical Practice* (CSAT, 2009).

Acamprosate was FDA approved in early 2005, but has been available in Europe and other countries for over 10 years. Acamprosate appears to work through the potentiation of the GABA system and antagonism of glutamate and holds promise for reduction of alcohol craving and preventing relapse. It is considered nonpsychoactive, has minimal drug interactions, and does not produce tolerance or withdrawal symptoms even if the person uses alcohol when taking the medication.

Acamprosate does not appear to be effective in persons who are less than moderately motivated to abstain from alcohol use. Because of low bioavailability (the degree and rate at which the medication is absorbed in the body), it is typically taken on a three times daily dosing schedule. Outcome studies indicate that acamprosate is best at increasing complete abstinence from alcohol, or increasing the time before the first drink (relapse). The profile of the person for whom acamprosate would be selected is one seeking complete abstinence and who is moderately to highly motivated to abstain from alcohol use.

Lower down the list of treatment options is topiramate, an anticonvulsant (not FDA approved for treatment of AUDs) that at higher doses can cause sedation and confusion. Johnson et al. (2007) studied the use of topiramate with an enhancement intervention compared to placebo with patients who

[27] *acetaldehyde*: A chemical compound produced when the body metabolizes alcohol; the liver enzyme, alcohol dehydrogenase, converts ethanol into *acetaldehyde*, which is then further converted into the harmless acetic acid by *acetaldehyde* dehydrogenase.

[28] *psychoactive*: Substances or drugs that affect the mind, especially mood, thought, or perception.

drank heavily. The study found that 300 mg of topiramate daily was significantly better than placebo regarding decrease in percentage of heavy drinking days. When taking topiramate it is important for persons to maintain adequate hydration to minimize the risk of developing nephrolithiasis.

USUAL DOSE & FREQUENCY

All medications have specific doses and frequencies. The physician will specify the exact amount of medication and when it should be taken; this information is provided on the prescription bottle. Disulfiram (as any other medication) should never be given to people without their full knowledge or when they are intoxicated. It should not be given until the person has abstained from alcohol for at least 12 hours. Persons should also be instructed to avoid the use of alcohol containing products including perfumes, colognes, and mouthwashes. A daily, uninterrupted dose of disulfiram is continued until the person, in consultation with his/her physician, has decided that he or she has reorganized his or her life to maintain recovery. Maintenance therapy may be required for months, years, or for the rest of their lives.

Naltrexone in its oral form is usually taken once a day but can be taken at a higher dose every second or third day. It is usually started at full dose. The injectable form of naltrexone is taken once a month. Because of acamprosate's low bioavailability, it must be taken as two pills three times a day with each dose separated by at least four hours.

People should continue to take naltrexone, until they, in consultation with their physician, have decided that they have reorganized their life to maintain recovery. Maintenance therapy may be required for months, years, or for the rest of their lives.

POTENTIAL SIDE EFFECTS

Potential side effects for disulfiram (rare at lower doses, mostly occur at higher doses > 500 mg day):

- Dark urine
- Drowsiness
- Eye pain
- Fatigue
- Erectile dysfunction
- Indigestion
- Inflammation of optic nerve
- Jaundice
- Light-colored stool
- Liver inflammation
- Loss of vision
- Psychotic reactions
- Skin rashes, itching
- Tingling sensation in arms and legs

Potential side effects for acamprosate (Side effects on therapeutic doses of acamprosate are rare, other than mild transient gastrointestinal symptoms during the first week):

- Agitation
- Coma
- Confusion
- Decreased urine output
- Depression
- Diarrhea
- Dizziness
- Headache
- Irritability and hostility
- Lethargy
- Muscle twitching
- Nausea
- Rapid weight gain
- Seizures
- Swelling of face, ankles or hands
- Unusual tiredness or weakness

EMERGENCY CONDITIONS

An overdose of any substance use disorder treatment medication is always considered an emergency and treatment should be sought immediately.

CAUTIONS

- Doctors and pharmacists should be told about all medications being taken and dosage, including over-the-counter preparations, vitamins, minerals, and herbal supplements (such as St. John's wort, echinacea, ginkgo, ginseng, etc.).
- People taking disulfiram should be warned to avoid even small amounts of alcohol in other food products or "disguised forms" as this will cause a reaction (such as vanilla, sauces, vinegars, perfumes, cold and cough medicines, mouthwashes, aftershave lotions, liniments, etc.).
- People taking disulfiram should be warned that consuming even small amounts of alcohol will produce flushing, throbbing in head and neck, headache, difficulty breathing, nausea, vomiting, sweating, thirst, chest pain, rapid heart rate, blurred vision, dizziness, and confusion.
- People taking naltrexone should be warned that if they are dependent on opioids, taking these medications will cause opioid withdrawal for up to three days and block the effect of any opioids taken for up to three days.

SPECIAL CONSIDERATIONS FOR PREGNANT WOMEN

Propranolol, labetalol, and metoprolol are the beta-blockers of choice for treating high blood pressure during pregnancy (McElhatton, 2001). However, the impact of using them for alcohol detoxification during pregnancy is unclear.

For all women of childbearing age who may be or think they may be pregnant, the physician should discuss the safety of these medications before starting, continuing, or discontinuing medication treatment. Practitioners may have a role in encouraging this discussion by suggesting their clients talk with the prescribing physician.

Opioid Use Disorders Treatment Medications

GENERIC	BRAND
Opioid withdrawal agents	
buprenorphine*	Buprenex*, Butrans*, Subutex*
buprenorphine and naloxone*	Suboxone*, Zubsolv*
clonidine	Catapres
methadone*	Dolophine*, Methadose*, Methadose Diskets*, Methadose Intensol*
naltrexone*	ReVia*
naltrexone extended-release injection*	Vivitrol*
Opioid maintenance agents	
buprenorphine*	Buprenex*, Butrans*, Subutex*
buprenorphine and naloxone*	Suboxone*, Zubsolv*
methadone*	Dolophine*, Methadose*, Methadose Diskets*, Methadose Intensol*

**FDA approved for treatment of Opioid Use Disorder (OUD).*

PURPOSE

Medications for opioid withdrawal and maintenance are a key component in the stabilization of persons with Opioid Use Disorders (OUDs). Appropriate use of these medications have shown marked ability to decrease illness, crime, and deaths in this population. Methadone maintenance treatment is extensively researched. See TIP 45: *Detoxification and Substance Abuse Treatment* (CSAT, 2006) and TIP 43*: Medication-Assisted Treatment for Opioid Addiction in Opioid Treatment Programs* (CSAT, 2005).

Opioid withdrawal: Mild opioid withdrawal can be treated with clonidine, a medication typically used for the treatment of high blood pressure. Clonidine may be used ("off label," as it is not FDA approved for treatment of OUDs) in combination with sedatives such as benzodiazepines to attenuate withdrawal symptoms. Major opioid withdrawal is usually treated with either an equivalent dose of methadone gradually decreased over time, or more recently, with an initial dose of buprenorphine, followed in 2–4 hours with a second dose, if indicated. Over the next two days, the dose of buprenorphine/naloxone can be increased. With the exception of pregnant women, for most patients the combination buprenorphine/naloxone is recommended (pregnant women who are determined to be appropriate candidates for buprenorphine treatment should be inducted and maintained on buprenorphine monotherapy). The objective of opioid withdrawal treatment is to stabilize the patient as rapidly as possible, to minimize any withdrawal symptoms, and to eliminate further use of illicit opioids. Only after a patient has completely discontinued use of illicit opioids should the dose-reduction phase begin. Specific dosage requirements for methadone and buprenorphine must be determined on an individual basis.

Opioid maintenance agents: Methadone is a synthetic, long-acting μ-agonist medication used in the treatment of opioid use disorders. It has been used in the U.S. for maintenance treatment of opioid use disorder since the 1960s. When used in proper doses, methadone stops the cravings but does not create euphoria, sedation, or an analgesic[29] effect. Many people who have been addicted to heroin have returned to a productive life because of methadone treatment programs. **Methadone** also is occasionally used to

[29] *analgesic*: Producing relief or insensibility to pain without loss of consciousness.

provide relief for specific types of pain (See also *Narcotic and Opioid Analgesics*, p. 30).

Buprenorphine, or **Subutex**, is a prescription medication approved in 2002 for treating opioid use disorder. Buprenorphine or methadone can be used for both opioid withdrawal and as a substitute for opioids in long-term treatment. Buprenorphine is the first medication available to doctors for use in their office-based practice. As a partial μ-agonist, buprenorphine at low doses acts like methadone and satisfies the dependent person's need for an opioid to avoid painful withdrawal. It does not provide the user with the euphoria or rush typically associated with use of other opioids or narcotics. At moderate to high doses, it can precipitate opioid withdrawal in persons high in opioids, nevertheless it is considered safer in overdose than methadone.

Suboxon and **Zubsolv** are buprenorphine combined with naloxone, a narcotic antagonist[30] used to reverse the effects of opioids. The combination of buprenorphine with naloxone is also approved for treating opioid use disorder and offers the same benefits as those previously stated for buprenorphine.

Naltrexone completely blocks the pleasurable reinforcement that comes from opioids. This medication is beginning to be more widely used for alcohol relapse prevention (see pp. 36–37).

USUAL DOSE & FREQUENCY

All medications have specific doses and frequencies. The physician will specify the exact amount of medication and when it should be taken; this information is provided on the prescription bottle.

Naltrexone in its oral form is usually taken once a day but can be taken at a higher dose every second or third day. It is usually started at full dose. The injectable form of naltrexone is taken once a month.

Buprenorphine combined with naloxone is given as a sublingual tablet (it is absorbed under the tongue). It is not absorbed if swallowed or chewed. If injected intravenously, buprenorphine will cause opioid withdrawal. Buprenorphine can be given by prescription and does not require daily attendance at a clinic. This is an advantage for persons who do not live near a methadone clinic.

People should continue to take naltrexone, or buprenorphine until they, in consultation with their physician, have decided that they have reorganized their life to maintain recovery. Maintenance therapy may be required for months, years, or for the rest of their lives.

POTENTIAL SIDE EFFECTS

Potential side effects for opioid treatment medications (See also *Narcotic and Opioid Analgesics*, p. 30):

- Abdominal cramps
- Body aches lasting 5–7 days
- Diarrhea
- Dizziness
- Fatigue
- Headache
- Insomnia
- Nausea
- Nervousness
- Opioid withdrawal (in some cases)
- Runny eyes and nose
- Severe anxiety
- Vomiting

EMERGENCY CONDITIONS

An overdose of any substance use disorder treatment medication is always considered an emergency and treatment should be sought immediately.

[30] *antagonist*: A substance that blocks the normal physiological function of a receptor site in the brain.

CAUTIONS

- Doctors and pharmacists should be told about all medications being taken and dosage, including over-the-counter preparations, vitamins, minerals, and herbal supplements (such as St. John's wort, echinacea, ginkgo, ginseng, etc.).
- People taking opioid medications should not increase or decrease their dose unless this has been *checked with their physician and a change is ordered*.
- People taking opioid medications are particularly vulnerable to adverse medical consequences if they concurrently use alcohol and/or street drugs.
- People taking naltrexone should be warned that if they are dependent on opioids, taking these medications will cause opioid withdrawal for up to three days and block the effect of any opioids taken for up to three days.

SPECIAL CONSIDERATIONS FOR PREGNANT WOMEN

A National Institutes of Health consensus panel recommended methadone maintenance as the standard of care for pregnant women with opioid dependence. Pregnant women should be maintained on an adequate (i.e., therapeutic) methadone dose. An effective dose prevents the onset of withdrawal for 24 hours, reduces or eliminates drug craving, and blocks the euphoric effects of other narcotics. An effective dose usually is in the range of 50–150mg (Drozdick et al., 2002). Dosage must be individually determined, and some pregnant women may be able to be successfully maintained on less than 50mg while others may require much higher doses than 150mg. The dose often needs to be increased as a woman progresses through pregnancy, due to increases in blood volume and metabolic changes specific to pregnancy (Drozdick et al., 2002; Finnegan & Wapner, 1988).

Generally, dosing of methadone is for a 24-hour period. However, because of metabolic changes during pregnancy it might not be possible to adequately manage a pregnant woman during a 24-hour period on a single dose. Split dosing (giving half the dose in the morning and half in the evening), particularly during the third trimester of pregnancy, may stabilize the woman's blood methadone levels and effectively treat withdrawal symptoms and craving.

Women who are on methadone may breastfeed their infant(s). Very little methadone comes through breast milk. The American Academy of Pediatrics (AAP) Committee on Drugs lists methadone as a "maternal medication usually compatible with breastfeeding" (AAP 2001, pp. 780–781).

The Federal government mandates that prenatal care be available for pregnant women on methadone. It is the responsibility of treatment providers to arrange this care. More than ever, there is need for collaboration involving obstetric, pediatric, and substance use disorders treatment providers. Comprehensive care for the pregnant woman who is opioid dependent must include a combination of methadone maintenance, prenatal care, and substance use disorder treatment. While it is not recommended that pregnant women who are maintained on methadone undergo detoxification, if these women require detoxification, the safest time is during the second trimester. In contrast, it is possible to detoxify women dependent on heroin who are abusing illicit opioids by using a methadone taper.

Buprenorphine has been examined in pregnancy and appears to have a low propensity to contribute to birth defects but it may be associated with a withdrawal syndrome in the newborn (Jones & Johnson, 2001). Buprenorphine has not yet been approved for use with this population. More data are

needed about the safety and effectiveness of buprenorphine with pregnant women.

Naloxone should not be given to a pregnant woman even as a last resort for severe opioid overdose. Withdrawal can result in spontaneous abortion, premature labor, or stillbirth (Weaver, 2003).

For all women of childbearing age who may be or think they may be pregnant, the physician should discuss the safety of these medications before starting, continuing, or discontinuing medication treatment. Practitioners may have a role in encouraging this discussion by suggesting their clients talk with the prescribing physician.

Tobacco Use Disorders Treatment Medications

GENERIC	BRAND
*Nicotine Replacement Therapies (NRT)**	
nicotine patch/ transdermal nicotine	Nicoderm CQ, Nicotrol, Habitrol, Prostep
nicotine polacrilex gum	Nicorette, Nicorelief, Thrive
nicotine polacrilex	Commit, Nicorelief, Nicorette lozenges
nicotine inhaler	Nicotrol Inhaler
nicotine nasal spray	Nicotrol NS
Pharmacotherapies for Smoking Cessation	
varenicline*	Chantix*
bupropion*	Zyban*
nortriptyline	Aventyl, Pamelor
clonidine	Catapres

**FDA approved for Smoking Cessation.*

PURPOSE

Complete long-term abstinence from all nicotine containing products is the goal of tobacco cessation therapies. Medications and products for tobacco cessation assist clients with nicotine dependence[31] to achieve abstinence by alleviating or reducing common nicotine withdrawal symptoms (irritability, anxiety, insomnia, etc.) and cravings. Numerous scientific studies have shown that it's easier for individuals to quit tobacco when supported by a medical or a mental health clinician. For this reason, recommended treatment strategies incorporate both behavioral counseling and pharmacotherapy. Nonetheless, pharmacotherapy is contraindicated for some specific populations (i.e., pregnant women, smoke-less tobacco users, light smokers, and adolescents). Empirically validated tobacco treatment strategies are available as cited in the *2008 Treating Tobacco Use and Dependence Guidelines* (DHHS 2008).

Nicotine Replacement Therapies (**NRT**) such as transdermal nicotine patch, nicotine polacrilex gum and lozenge, nicotine nasal spray, and nicotine inhaler are FDA-approved. These therapies reduce withdrawal symptoms and cravings by replacing nicotine that would be ingested through chewing tobacco or smoking cigarettes. Numerous clinical trials involving NRT have demonstrated the effectiveness of these products for smoking cessation.

Bupropion, as an antidepressant, can help with withdrawal anxiety and depression. Sustained-release bupropion (bupropion SR) is one of two non-nicotine pharmaceutical aids that are FDA-approved for smoking cessation. This agent is thought to affect dopamine[32] and norepinephrine[33] levels, and blocks nicotinic acetylcholinergic receptors[34], thereby decreasing cravings for cigarettes and symptoms of nicotine withdrawal. The use of bupropion roughly doubles cessation rates relative to placebo, and the combination of bupropion with the nicotine patch has shown higher quit rates than using the patch alone.

[31] *nicotine dependence*: Nicotine dependence is a recognized mental health disorder that is often overlooked by counselors. This addiction significantly reduces the overall quality-of-life and is considered the deadliest yet most preventable disease to be treated. Cigarette smoking is a primary cause of cancers of the esophagus, lung, throat, mouth and is associated with the development of cancers of the bladder, cervix, kidneys, pancreas, stomach, and some leukemias. Smoking is also a major cause of heart disease, bronchitis, emphysema, and stroke. Nicotine, the addictive chemical in cigarettes and other forms of tobacco, crosses the blood-brain barrier and activates the brain's reward center. This causes the brain to release noradrenaline and dopamine, which act as stimulants (implicated in mood, memory, and sense of well-being). Nicotine remains active for 20-40 minutes in the brain, and then withdrawal symptoms begin, leading to cravings for more nicotine.

[32] *dopamine*: A type of neurotransmitter in the brain.

[33] *norepinephrine*: A type of neurotransmitter in the brain.

[34] *acetylcholinergic receptors*: A type of neurotransmitter receptor in the brain activated by the neurotransmitter acetylcholine.

Varenicline is a more recently FDA-approved smoking cessation medication and the first in its class targeting specifically the neurobiology of nicotine use disorder. It reduces the smoker's craving for nicotine by binding to nicotine receptors in the brain and thereby reducing withdrawal symptoms as well as resulting in a less satisfying smoking experience. Smokers using varenicline have better rates of smoking cessation compared to those who use bupropion. Varenicline offers a new option for those who cannot tolerate the adverse effects associated with NRT and bupropion, and represents an alternative for clients with contraindications to such therapies.

Nortriptyline, a tricyclic antidepressant, and clonidine, an antihypertensive agent, are also considered potential treatment options. However, because of tolerability concerns they are relegated to second-line treatment considerations.

USUAL DOSE & FREQUENCY

All medications have specific doses and frequencies. The physician will specify the exact amount of medication and when it should be taken; this information is provided on the prescription bottle.

Some Nicotine Replacement Therapy (NRT) medications can be obtained without a prescription, including the nicotine patch, gum, and lozenge. Specific information on how to use NRT products correctly, recommended dosing schedules, symptoms of overdose, and proper storage/disposal of the products are included on the product label or inside the package.

The nicotine patch is available in three strengths and a "step-down" approach is used: 21 mg for 6 weeks, then 14 mg for 2 weeks, then 7 mg for 2 weeks. For those who smoke less than one pack a day, consider starting at 14 mg dose. A new patch needs to be reapplied each day, at roughly the same time each day.

The nicotine polacrilex gum and lozenge are offered in 2 milligrams (mg) and 4 mg. Individuals who smoke fewer than 25 cigarettes per day should initiate therapy with the 2 mg strength, and heavier smokers should initiate with the 4 mg strength. During the initial 6 weeks of therapy, one piece of gum should be chewed every 1 to 2 hours while awake; up to at least nine pieces of gum daily. The gum should be used for up to 12 weeks and no more than 24 pieces should be chewed a day. A "chew and park" technique is necessary for nicotine to absorb correctly and food or beverages should be avoided 15 minutes before or after using the nicotine gum.

Unlike other forms of NRT, which are dosed based on the number of cigarettes smoked per day; the recommended dosage of the nicotine lozenge is based on the "time to first cigarette" of the day. Some studies suggest that the best indicator of nicotine dependence is having a strong desire or need to smoke soon after waking. Clients who smoke their first cigarette of the day within 30 minutes of waking are likely to be more highly dependent on nicotine and require higher dosages than those who delay smoking for more than 30 minutes after waking. During the initial 6 weeks of therapy, clients should use one lozenge every 1 to 2 hours while awake; at least nine lozenges daily. Clients can use additional lozenges (up to 5 lozenges in 6 hours or a maximum of 20 lozenges per day) if cravings occur between the scheduled doses. The lozenges should be used for up to 12 weeks with no more than 20 lozenges used a day. Lozenges should be allowed to dissolve in the mouth and food or beverages should be avoided 15 minutes before or after using the nicotine lozenge.

Bupropion should be started 7 to 14 days before a targeted smoking cessation date. Generally, for the first 3 days of treatment, individuals take 150 mg, then 150 mg twice a day for 7 to 12 weeks, and for some individ-

uals, up to 6 months to increase the likelihood of long-term tobacco cessation.

The approved course of varenicline treatment is 12 weeks; however, an additional 12 weeks of treatment may increase the likelihood of long-term smoking cessation for some individuals. For the first 3 days of treatment, individuals take 0.5 mg once a day, followed by 0.5 mg twice a day for the next four days, and then 1 mg twice a day for the remainder of the treatment period.

For certain groups of smokers, it may be appropriate to continue NRT treatment or pharmacotherapies for periods longer than is usually recommended. In general, the more intense the treatment for tobacco cessation (e.g., combined use of NRT and pharmacotherapies), the higher the likelihood of successful cessation. Specific combinations of first line medications shown to be effective include the nicotine patch and bupropion SR, the nicotine patch and the inhaler, and long-term nicotine patch (greater than 14 weeks) and *ad libitum* NRT use. Varenicline is not recommended for use in combination with NRT because of its nicotine antagonist properties.

While NRT replaces the nicotine that the patient had while smoking, bupropion and varenicline are medications that aid in quitting. The underlying desire to quit must be present or bupropion and varenicline will have little to no effect on the patient that is trying to quit.

POTENTIAL SIDE EFFECTS

*Potential side effects for NRT and pharmacotherapies for smoking cessation**

Nicotine patch: skin reactions (i.e., itching, burning, redness or rash at patch site) are usually mild and often resolved by rotating patch site. Other side effects include insomnia, nausea, and/or vivid dreams.

Nicotine gum: mouth soreness, hiccups, indigestion, jaw muscle aches. Most of these are mild and subside with continued use of the gum.

Nicotine lozenges: nausea, hiccups, throat irritation, heartburn. Use of the 4 mg dose has been associated with increased rates of headaches and coughing.

Bupropion: upset stomach, insomnia, headache. Use with caution if there is a history of seizures or an eating disorder as use has been associated with seizure activity.

Varenicline: nausea, trouble sleeping, abnormal/vivid/strange dreams, increase in suicidal thoughts in some patients.

*See FDA package insert for each product for a more complete list of side effects and black box warnings. It is strongly recommended to read FDA insert thoroughly before beginning treatment.

EMERGENCY CONDITIONS

An overdose of any substance use disorder treatment medication is always considered an emergency and treatment should be sought immediately.

Symptoms of a nicotine overdose may include nausea, vomiting, diarrhea, stomach pain, cold sweats, headache, dizziness, problems with hearing or vision, confusion, an irregular heartbeat, chest pain, seizures, and death.

CAUTIONS

- Doctors and pharmacists should be told about all medications being taken and dosage, including over-the-counter preparations, vitamins, minerals, and herbal supplements (such as St. John's wort, echinacea, ginkgo, ginseng, etc.).
- Smoking can have an effect on the way the body processes other prescribed medications. Aromatic hydrocarbons found in tar in cigarettes stimulates enzymes in the liver (notably CYP450 1A2), and fluctuations in

an individual's smoking pattern can result in higher or lower doses of medications needed to reach therapeutic levels.

- Although studies have now documented the lack of association between the nicotine patch and acute cardiovascular events, even with individuals who continued to smoke while on the patch, all NRT products should be used with caution for individuals who had a recent (within 2 weeks) myocardial infarction (MI)[35], those with severe arrhythmias, or those with unstable angina pectoris.[36]
- NRT products should be properly disposed of to insure safety of children and pets. Nicotine on hands can get into nose or eyes, causing stinging and redness. Wash hands with soap and water after handling the patch.
- Because seizures have been reported in 0.1% of patients, bupropion is contraindicated in individuals who have a history of seizure disorder, have a current or prior diagnosis of anorexia[37] or bulimia[38], are currently using another form of bupropion, or are currently using or have used a Monoamine Oxidase (MAO) Inhibitor within the past two weeks. Other factors that might increase the odds of seizure and are classified as warnings for this medication include a history of head trauma, central nervous system tumor, the presence of severe hepatic cirrhosis, and concomitant use of medications that lower the seizure threshold. Bupropion can be used safely in combination with NRT and may be beneficial for use in clients with underlying depression.
- Although varenicline is well tolerated in most individuals, recent case reports describe exacerbations of existing psychiatric illness in clients who took varenicline prompting the FDA to add a warning regarding the use of varenicline in February 2008. Specifically, the warning notes that depressed mood, agitation, changes in behavior, suicidal ideation, and suicide have been reported in clients attempting to quit smoking while using varenicline. Patients who have a change in personality, increase in anger or thoughts of suicide should be immediately referred back to their doctor.
- Because varenicline is eliminated almost entirely unchanged in the urine, it should be used with caution in clients with severe renal dysfunction.

SPECIAL CONSIDERATIONS FOR PREGNANT WOMEN

Nicotine use during pregnancy has been associated with low birth weight. Although nicotine replacement therapy (NRT) is generally contraindicated during pregnancy, some health professionals argue the use of NRT is a lower risk than continuing to smoke during pregnancy, though discussion should occur between the physician and patient to determine if NRT or continuation of smoking is the greater risk.

For all women of childbearing age who may be or think they may be pregnant, the physician should discuss the safety of these medications before starting, continuing, or discontinuing medication treatment. Practitioners may have a role in encouraging this discussion by suggesting their clients talk with the prescribing physician.

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[35] *myocardial infarction (MI):* Myocardial infarction, more commonly known as a heart attack, is a medical condition that occurs when the blood supply to a part of the heart is interrupted.

[36] *unstable angina pectoris*: commonly known as angina, is chest pain due to ischemia (a lack of blood and hence oxygen supply) of the heart muscle, generally due to obstruction or spasm of the coronary arteries (the heart's blood vessels).

[37] *anorexia*: An eating disorder marked by an extreme fear of becoming overweight that leads to excessive dieting to the point of serious ill-health and sometimes death.

[38] *bulimia*: A condition in which periods of overeating are followed by under-eating, use of laxatives, or self-induced vomiting. It is associated with depression and anxiety about putting on weight.

Other Substance Use Disorders Treatment Medications

Stimulant intoxication: Agitation, paranoia and psychosis are treated with antipsychotics, often combined with benzodiazepines. Both alcohol and stimulant intoxication together commonly appear to cause these symptoms.

Stimulant withdrawal: There are no standard effective agents to treat stimulant withdrawal, though dopamine-enhancing agents such as amantadine, bupropion, and desipramine have been tried with mixed results. This area has not been well researched.

Stimulant relapse prevention: Again, dopamine-enhancing agents such as bupropion and desipramine have mixed results. The National Institute on Drug Abuse (NIDA) is researching agents that might alter how stimulants act on a person, including the development of "inoculation" agents that might inactivate stimulants.

Club Drugs: Little research has occurred in this area. There are reports that SSRIs may be protective of the damage caused to nerve cells by some of these drugs. Antipsychotics and sedatives are used to treat induced psychoses associated with club drug use.

Marijuana: Recently, a withdrawal syndrome to marijuana dependence has been described and validated. Medications for treating this syndrome have not been adequately tested. THC[39], the chief intoxicant in marijuana, is a strong anticholinergic agent and is sedating. Therefore some clinicians have used moderate doses of the older tricyclic antidepressants (e.g., amitriptyline or imipramine) to treat withdrawal from marijuana as they also have anticholinergic and sedating qualities but do not cause a high, nor are they abused.

USUAL DOSE & FREQUENCY

All medications have specific doses and frequencies. The physician will specify the exact amount of medication and when it should be taken; this information is provided on the prescription bottle.

EMERGENCY CONDITIONS

An overdose of any substance use disorder treatment medication is always considered an emergency and treatment should be sought immediately.

CAUTIONS

- Doctors and pharmacists should be told about all medications being taken and dosage, including over-the-counter preparations, vitamins, minerals, and herbal supplements (such as St. John's wort, echinacea, ginkgo, ginseng, etc.).

SPECIAL CONSIDERATIONS FOR PREGNANT WOMEN

For all women of childbearing age who may be or think they may be pregnant, the physician should discuss the safety of these medications before starting, continuing, or discontinuing medication treatment. Practitioners may have a role in encouraging this discussion by suggesting their clients talk with the prescribing physician.

[39] *THC*: *Tetrahydrocannabinol*: An active chemical from hemp plant resin that is the chief intoxicant in marijuana.

Tips for Communicating with Physicians about Clients and Medication

Send a written report.

The goal is to get your concerns about your client's health included in the client's medical record. When information is in a medical record, it is more likely to be acted on. Records of phone calls and letters may or may not be placed in the chart.

Make it look like a report–and be brief.

Include date of report, client name and Social Security Number. Most medical consultation reports are one page. Longer reports are less likely to be read. Include and prominently label sections:

Presenting Problem

Assessment

Treatment and Progress

Recommendations and Questions

Keep the tone neutral.

Provide details about the client's use and/or misuse of prescription medications. Avoid making direct recommendations about prescribed medications. Allow the physician to draw his/her own conclusions. This will enhance your alliance with the physician and makes it more likely that he/she will act on your input.

Do your best to become a "team."

When the physician does not respond.

Professional duty dictates that a report should be updated whenever a client's condition or situation changes in a manner thought to affect the client's general health and/or medical care. Continue attempts to coordinate care when it is in the client's best interest even if the physician appears not to respond.

Download The Substance Use Disorder Treatment Coordination Report (available in English and Spanish)–www.ATTCnetwork.org/midamerica

References

ACOG (2009). Practice Bulletin. Clinical Management Guidelines for Obstetrician-Gynecologists. Use of Psychiatric Medications during Pregnancy and Lactation. *FOCUS 7*(3), p. 395. Retrieved on November 08, 2013 from: http://focus.psychiatryonline.org/article.aspx?articleID=52963

Adams, J.B., & Wacher, A. (1968). Specific changes in the glycoprotein components of seromucoid in pregnancy. *Clinica Chimica Acta: International Journal of Clinical Chemistry, 21(1)*, 155-157.

American Academy of Pediatrics, Committee on Drugs (2001). The transfer of drugs and other chemicals into human milk. Pediatrics, 108(3), 776-789.

Bogart, G. T., & Ott, C. A. (2011). Abuse of second-generation antipsychotics: What prescribers need to know. *Current Psychiatry, 10*(5), 77-79.

Boyer, E.W., & Shannon, M (2005). The serotonin syndrome. *New England Journal of Medicine, 352* (11), 1112–20. doi:10.1056/NEJMra041867. PMID 15784664.

Briggs, G.G., Freeman, R. K., & Yaffe, S.J. (2002). *Drugs in Pregnancy and Lactation*. 6th ed. Baltimore, Md: Lippincott Williams & Wilkins.

Buhrich, N., Weller, A., & Kevans, P. (2000). Misuse of anticholinergic drugs by people with serious mental illness. *Psychiatric Services, 51(7),* 928-929.

Center for Substance Abuse Treatment (2005). Medication-Assisted Treatment for Opioid Addiction in Opioid Treatment Programs. Treatment Improvement Protocol (TIP) Series 43. DHHS Publication No. (SMA) 12-4214. Rockville, MD: Substance Abuse and Mental Health Services Administration.

Center for Substance Abuse Treatment (2005). Substance Abuse Treatment for Persons with Co-Occurring Disorders. Treatment Improvement Protocol (TIP) Series 42. DHHS Publication No. (SMA) 05-3992. Rockville, MD: Substance Abuse and Mental Health Services Administration.

Center for Substance Abuse Treatment (2006). Detoxification and Substance Abuse Treatment. Treatment Improvement Protocol (TIP) Series 45. DHHS Publication No. (SMA) 06-4131. Rockville, MD: Substance Abuse and Mental Health Services Administration.

Center for Substance Abuse Treatment (2009). Incorporating Alcohol Pharmacotherapies into Medical Practice (CSAT 2009). Treatment Improvement Protocol (TIP) Series 49. DHHS Publication No. (SMA) 09-4380. Rockville, MD: Substance Abuse and Mental Health Services Administration.

Cohen, L.S. (1989). Psychotropic drug use in pregnancy. *Hospital & Community Psychiatry*, 40(6), 566-567.

Dean, M., Stock, B., Patterson, R.J., & Levy, G. (1980). Serum protein binding of drugs during and after pregnancy in humans. *Clinical Pharmacology and Therapeutics, 28(2),* 253-261.

Drozdick, J., III, Berghella, V., Hill, M., & Kaltenbach, K. (2002). Methadone trough levels in pregnancy. *American Journal of Obstetrics and Gynecology, 187*(5), 1184-1188.

Egger, J. F. M. D., & Hebert, C. M. D. (2011). Buspirone: Anxiolytic, Antidepressant, or Neither? *Psychiatric Annals, 41*(3), 166-175. doi: http://dx.doi.org/10.3928/00485713-20110224-06

Farach, F. J., Pruitt, L. D., Jun, J. J., Jerud, A. B., Zoellner, L. A., & Roy-Byrne, P. P. (2012). Pharmacological treatment of anxiety disorders: Current treatments and future directions. *Journal of Anxiety Disorders, 26*(8), 833-843. doi: http://dx.doi.org/10.1016/j.janxdis.2012.07.009

Finnegan, L.P., & Wapner, R.J. (1988). Narcotic addiction in pregnancy. In: Niebyl, J.R., ed. Drug Use in Pregnancy. 2d ed. Philadelphia: Lea & Febiger, pp. 203-222.

Ganrot, P.O. (1972). Variation of the concentrations of some plasma proteins in normal adults, in pregnant women and in newborns. *Scandinavian Journal of Clinical and Laboratory Investigation Supplementum, 124,* 83-88.

Garbis, H., & McElhatton, P.R. (2001). Psychotropic, sedative-hypnotic and Parkinson drugs. In*: Drugs During Pregnancy and Lactation: Handbook of Prescription Drugs and Comparative Risk Assessment: With Updated Information on Recreational Drugs*. New York: Elsevier, pp. 182-191.

Johnson, B. A., Rosenthal, N., Capece, J. A., Wiegand, F., Mao, L., Beyers, K., McKay, A., (...), Swift, R. M. (2007). Topiramate for treating alcohol dependence: A randomized controlled trial. *Journal of the American Medical Association, 298*(14), 1641-1651.

Jones, H.E., & Johnson, R.E. (2001). Pregnancy and substance abuse. *Current Opinion in Psychiatry, 14*, 187-193.

Kamin, J., Manwani, S., & Hughes, D. (2000). Extrapyramidal side effects in the psychiatric emergency service. *Psychiatric Services, 51*(3).

Kreyenbuhl, J., Buchanan, R. W., Dickerson, F. B., & Dixon, L. B. (2010). The schizophrenia patient outcomes research team (PORT): Updated treatment recommendations 2009. *Schizophrenia Bulletin, 36*(1), 94-103.

Kuhnz, W., Koch, S., Helge, H., & Nau, H. (1988). Primidone and phenobarbital during lactation period in epileptic women: Total and free drug serum levels in the nursed infants and their effects on neonatal behavior. *Developmental Pharmacology and Therapeutics, 11*(3), 147-154.

Lader, M. (2011). Benzodiazepines revisited—will we ever learn? *Addiction, 106*(12), 2086-2109. doi: 10.1111/j.1360-0443.2011.03563.x

Leucht S, Cipriani A, Spineli L, Mavridis D, Örey D, Richter F, et al. (2013). Comparative efficacy and tolerability of 15 antipsychotic drugs in schizophrenia: a multiple-treatments meta-analysis. *The Lancet* 382(9896):951–62. Available from: http://www.sciencedirect.com/science/article/pii/S0140673613607333

Lichtigfeld, F. J., & Gillman, M. A. (1998). Antidepressants are not drugs of abuse or dependence. *Post Graduate Medicine Journal, 74,* 529-322.

McElhatton, P. (2001). Heart and circulatory system drugs. In: Schaefer, C. Drugs During Pregnancy and Lactation: Handbook of Prescription Drugs and Comparative Risk Assessment. Amsterdam: Elsevier Science B.V., pp. 116-131.

Mortola, J.F. (1989). The use of psychotropic agents in pregnancy and lactation. *Psychiatric Clinics of North America*, 12, 69-88.

Mueser, K. T., & Jeste, D. V. Eds. (2008). *Clinical Handbook of Schizophrenia*. New York, NY The Guilford Press. A Division of Guilford Publications, Inc. p. 168

Perucca, E., & Crema, A. Plasma protein binding of drugs in pregnancy (1982). *Clinical Pharmacokinetics, 7*(4), 336-352.

Pond, S.M., Kreek, M.J., Tong, T.G., Raghunath, J., & Benowitz, N.L. (1985). Altered Methadose pharmacokinetics in methadone-maintained pregnant women. *Journal of Pharmacology and Experimental Therapeutics, 233*(1), 1-6.

Reeves, R.R., & Brister, J.C. (2007). Additional evidence of the abuse potential of quetiapine. *Southern Medical Journals*, 100, 834-6.

Robert, E., Reuvers, M., & Shaefer, C. (2001). Antiepileptics. In: Schaefer, C.H., ed. *Drugs During Pregnancy and Lactation: Handbook of Prescription Drugs and Comparative Risk Assessment: With Updated Information on Recreational Drugs*. Amsterdam: Elsevier, pp. 46-57.

Ries, R.K. (2014). Principles of Addiction Medicine. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins.

Sernyak, M.J., Leslie, D.L., Alarcon, R.D., Losonczy, M.F., & Rosenheck, R. (2002). Association of diabetes mellitus with use of atypical neuroleptics in the treatment of schizophrenia. *American Journal of Psychiatry*, 159(4), 561-566.

Stahl, S. M. (2008). *Stahl's Essential Psychopharmacology: Neuroscientific basis and practical application. 3rd ed.* New York, N.Y.: Cambridge University Press.

Stahl, S. M. (2011). *The Prescriber's Guide (Stahl's Essential Psychopharmacology)*: Cambridge University Press; 4th ed.

Substance Abuse and Mental Health Services Administration SAMHSA (2006). Drug Abuse Warning Network, 2006: National Estimates of Drug-Related Emergency Department Visits. Substance Abuse and Mental Health Services Administration. Retrieved September 2013 from: http://www.samhsa.gov/data/DAWN/files/ED2006/DAWN2k6ED.htm

Sullivan, J.T.; Sykora, K.; Schneiderman, J.; Naranjo, C.A.; & Sellers, E.M. (1989). Assessment of alcohol withdrawal: The revised Clinical Institute Withdrawal Assessment for Alcohol scale (CIWA-Ar). *British Journal of Addiction 84*:1353-1357.

Sutton, L.R., & Hinderliter, S.A. (1990). Diazepam abuse in pregnant women on methadone maintenance: Implications for the neonate. *Clinical Pediatrics, 29,* 108-111.

Warner, C.H., Bobo, W., Warner, C., Reid, S., & Rachal, J. (2006). Antidepressant Discontinuation Syndrome. *Journal of American Family Physicians, 74,* 449-57.

Weaver, M.F. (2003). Perinatal addiction. In: Graham, A.W., Schultz, T.K., Mayo-Smith, M.F., Ries, R.K., and Wilford, B.B., eds. Principles of Addiction Medicine, 3rd ed. Chevy Chase, MD: American Society of Addiction Medicine, pp. 1231-1246.

Wimbiscus, M., Kostenki, O., & Malone, D. (2010). MAO inhibitors: Risks, benefits, and lore. *Cleveland Clinic Journal of Medicine, 77*(12), 859-861, 865, 872-873, 877-878, 882. doi: 10.3949/ccjm.77a.09103

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Acknowledgements

This 2014 edition was made possible because of the dedication and commitment of many individuals and organizations. It includes an adaptation of the 2004 edition that was modified and enhanced by CSAT for inclusion in their *TIP 42: Substance Abuse Treatment for Persons with Co-Occurring Disorders*.

The Mid-America ATTC gratefully acknowledges former contributors to earlier editions:

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Talking with Clients about their Medication

Untreated psychiatric problems are a common cause for treatment failure in substance use disorder treatment programs. Supporting clients with mental illness in continuing to take their psychiatric medications can significantly improve substance use disorder treatment outcomes.

Getting Started. Take 5-10 minutes every few sessions to go over these topics with your clients:

Remind them that taking care of their mental health will help prevent relapse.

Ask how their psychiatric medication is helpful.

Acknowledge that taking a pill every day is a hassle.

Acknowledge that everybody on medication misses taking it sometimes.

Do not ask if they have missed any doses, rather ask, *"How many doses have you missed?"*

Ask if they felt or acted different on days when they missed their medication.

Was missing the medication related to any substance use relapse?

Without judgment, ask *"Why did you miss the medication? Did you forget, or did you choose not to take it at that time?"*

For clients who forgot, ask them to consider the following strategies:

Keep medication where it cannot be missed: with the TV remote control, near the refrigerator, or taped to the handle of a toothbrush. Everyone has two or three things they do every day without fail. Put the medication in a place where it cannot be avoided when doing that activity, but always away from children.

Suggest they use an alarm clock set for the time of day they should take their medication. Reset the alarm as needed.

Suggest they use a Mediset: a small plastic box with places to keep medications for each day of the week, available at any pharmacy. The Mediset acts as a reminder and helps track whether or not medications were taken.

For clients who admit to choosing NOT to take their medication:

Acknowledge they have a right to choose NOT to use any medication.

Stress that they owe it to themselves to make sure their decision is well thought out. It is an important decision about their personal health and they need to discuss it with their prescribing physician.

Ask their reason for choosing not to take the medication.

Don't accept *"I just don't like pills*." Tell them you are sure they wouldn't make such an important decision without having a reason.

Offer as examples reasons others might choose not to take medication. For instance, they:

1. Don't believe they ever needed it; never were mentally ill
2. Don't believe they need it anymore; are cured
3. Don't like the side effects
4. Fear the medication will harm them
5. Struggle with objections or ridicule of friends and family members
6. Feel taking medication means they're not personally in control

Transition to topics other than psychiatric medications. Ask what supports or techniques they use to assist with emotions and behaviors when they choose not to take the medication.

General Approach: The approach when talking with clients about psychiatric medication is exactly the same as when talking about their substance use decisions.

Explore the triggers or cues that led to the undesired behavior (either taking drugs of abuse or not taking prescribed psychiatric medications).

Review why the undesired behavior seemed like a good idea at the time.

Review the actual outcome resulting from their choice.

Ask if their choice got them what they were seeking.

Strategize with clients about what they could do differently in the future.

Brief Counselor Strategies for Tobacco Users—the Five As*

ASK about tobacco use and past quit efforts

Get the conversation started:

"Do you currently use any form of tobacco? Have you used it in the past? How old were you when you started? Tell me about your efforts to quit. What helped, what didn't help?"

ADVISE abstinence

Advice should be:

Clear: "Quitting is the most important thing you can do for your health. Cutting down is not enough."

Strong: "You are more likely to die from smoking than from all other drugs and alcohol use combined."

Personalized: "You have powerful reasons to quit. For example..." [tie tobacco use in with current symptoms or health concerns].

ASSESS willingness for a quit attempt during next 30 days

Determine motivation level to quit:

"On a scale from 1 to 10, with 1 being 'not at all motivated' to 10 being 'extremely motivated,' how ready are you to quit in the next 30 days?"

If willing to make a quit attempt:

Communicate research in quitting, "Research shows that quitting is possible for all populations. In fact, more people have quit than are still smoking and about 80% of all Americans are smoke-free."

Discuss effective treatments available, such as nicotine replacement therapies (NRTs), medications, self-help resources (help lines or support groups), and counseling.

Initiate agreed upon treatment plan, "Let's come up with a plan."

If unwilling to make a quit attempt, provide motivational intervention (see Five Rs section)

ASSIST quit attempt effort

Develop a quit plan **(STAR)***:*

Set a specific quit date, ideally within two weeks, that has some meaning (e.g., anniversary, stress-free weekend)

Tell family, friends, coworkers and others about quitting, request extra support and understanding; ask other smokers in the household to not smoke inside; identify at least one non-smoker to talk to when tempted to smoke

Anticipate challenges that will occur including withdrawal symptoms, cravings, and high-risk situations

Remove environmental triggers (e.g., ashtrays, lighters); avoid smoking in 'favorite' places (e.g., car, dinner table, easy chair); limit smoking to uncomfortable places (e.g., outside); recommend visiting only smoke-free establishments

Provide problem-solving strategies and skills training:

Track tobacco use patterns (e.g., time, circumstances) and identify high risk situations:

- Internally—mood swings, negative self-talk, smoking urges
- Externally—drinking coffee, taking a break, watching TV, driving, seeing other smokers

Identify substitute behaviors to smoking and other cognitive behavioral activities for coping (e.g., keep hands busy with a 'worry stone;' chew gum; exercise; engage in 'self-soothing' activities such as warm bath, listen to soothing music; imagine telling people you are a non-smoker, practice asking others to not smoke around you or leave cigarettes around; change daily routine)

Provide basic information about smoking and successful quitting (e.g., educate on the addictive nature of smoking; discuss that even a single puff increases the likelihood of a full relapse; withdrawal symptoms typically peak within 1–2 weeks after quitting but may persist for months)

Recommend use of NRTs, tobacco cessation medications:

Explain how these products increase smoking cessation rates and reduce withdrawal symptoms and cravings

Provide materials on dosages, contraindications, side effects, etc.

Assist in obtaining prescription

ARRANGE follow-up help

Timing:

Schedule first follow-up within one week of quit date and a second follow-up within one month; schedule additional follow-ups as indicated, encouraging and allowing phone calls as needed

Make sure that NRTs, medications, and educational materials are received prior to quit date

If abstinent during follow-up:

Congratulate on success; consider giving a certificate or other reinforcement

Check on whether cravings increased for other substances (alcohol, other drugs)

Discuss relapse prevention

Start planning ahead for a smoke-free life

If slip or relapse occurred:

Normalize the difficulty in quitting

Reframe relapse as a learning experience and does not mean failure or necessitate a return to full tobacco use

Motivate to try to quit again immediately

Reassess and re-initiate quit plan

Brief Counselor Strategies for Tobacco Users Unwilling to Quit—the Five Rs*

RELEVANCE of quitting

Discuss the relevance of quitting for health and economic concerns:

Encourage identifying why quitting is personally relevant to him/her (health status, family or social situation, age, gender, prior quitting experiences, etc.)

Write down personal incentives for quitting, rank order reasons, focus on them as often as possible, carry around on card in cigarette pack

RISKS of continued use

Discuss short- and long-term impact to person and family:

Highlight risks specific to him/her and prioritize, "Spouses, children, and other people exposed to secondhand smoke are at higher risk to get colds, flu, ear infections, and lung infections than people who are not around secondhand smoke"

Inform him/her that reducing number of cigarettes, using alternative tobacco products (cigars), or switching brands will not eliminate risks

Discuss acute (e.g., harm to pregnancy) and long-term (e.g., lung and other cancers) risks

REWARDS of quitting

Discuss physical changes (some immediate) as a result of quitting and highlight those most relevant:

Pulmonary benefits:

- Carbon monoxide and oxygen levels in the blood return to normal after 8 hours
- Bronchial tubes relax, making it easier to breathe after 72 hours
- Cilia re-grow in lungs, increasing ability to fight infection after 1-9 months
- Coughing, sinus infection, and shortness of breath decrease after 1-9 months

Cardiac benefits:

- Blood pressure and body temperature returns to normal after 20 minutes
- Chance of heart attack decreases after only 24 hours
- Risk of coronary heart disease is half that of a smoker within 1 year
- Heart attack risk drops to near normal within 2 years
- Stroke risk is reduced after 5 years
- Risk of coronary heart disease is the same as non-smokers within 15 years

Reduced cancer risk benefits:

- Lung cancer death rates for a former pack per day smoker is cut in half after 5 years
- Risk of throat, mouth, and esophageal cancers is cut in half after 5 years
- Lung cancer death rate is similar to that of non-smokers within 10 years
- Pre-cancerous cells are replaced within 10 years

Other benefits:

- Expect to save $2000/year or more, list ideas for how to spend money saved
- Improved taste and smell, improved smell of home and car, reduce aged appearance
- Improved sleep, reduced anxiety, reduced depression, and improved sexual functioning after period of abstinence
- Strengthened sobriety from other addictive substances (when sobriety from those substances is already established)

Identify ROADBLOCKS to quitting

Encourage each individual to discuss his/her perceived barriers to quitting and offer strategies that address these challenges:

Examples of roadblocks could include fear of failure, weight gain, lack of support, mood or emotional problems, withdrawal symptoms, life circumstances, presence of another smoker in the household, enjoyment of tobacco, etc.

Use REPETITION

Use motivational interventions each session:

Repeat the Relevance, Risks, and Rewards

*The Five As and Five Rs are available in the 2008 update of the *Treating Tobacco Use and Dependence Guidelines* (DHHS 2008).

Notes

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Mid-America (HHS Region 7)

ATTC Addiction Technology Transfer Center Network

Funded by Substance Abuse and Mental Health Services Administration

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