



BENZODIAZEPINES

Alprazolam – Xanax

Clobazam (Onfi)

Clonazepam (Klonopin) –[Top 10 drugs for APS]

Clorazepate (Tranxene)

Chlordiazepoxide (Librium)

Diazepam (Valium)

Estazolam (Prosom)

Lorazepam (Ativan) –[Top 10 drugs for APS]

Oxazepam (Serax)

Temazepam(Restoril)

Traizolam (Halcion)



COMMONLY PRESCRIBED BENZODIAZEPINES	
AMBIEN	
ATIVAN	
HALCION	
KLONOPIN	
LUNESTA	
ROHYPNOL	
VALIUM	
XANAX	



COMMON GENERIC & BRAND BZD'S

About Benzos

Benzodiazepines are a class of drugs primarily used for treating anxiety, but they also are effective in treating several other conditions.

They act on the central nervous system, produce sedation and muscle relaxation and lower anxiety levels.

They tend to be classified by how long their effects last

- ultra-short-acting
- Short-acting
- Long acting

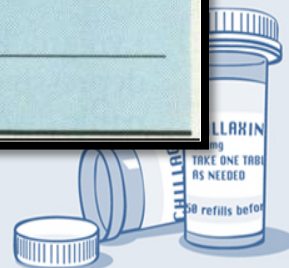
Due to their sedative properties, benzos have a high potential for abuse.

Table 1 — Classification of benzodiazepines, by potency and therapeutic indications

Potency	Therapeutic indications
Low	Very mild generalized anxiety or sleep disorder
Chlordiazepoxide	
Oxazepam	
Temazepam*	
Medium	Mild to moderate generalized anxiety disorder
Clorazepate	
Diazepam	
Flurazepam*	
Halazepam	
Prazepam	
High	Panic attacks, acute mania, severe generalized anxiety disorder associated with psychic or somatic symptoms and severe sleep disorder
Alprazolam	
Bromazepam	
Clonazepam	
Lorazepam	
Triazolam*	

*Approved as a hypnotic.

Benzodiazepines



Pharmacodynamics

study of what a drug does to the body

Pharmacology

science of drug action on biological systems

Anxiety and panic disorders supposedly result from a lack of GABA neurotransmitters in the brain.

Increasing the general GABA activity in the brain relieves the anxiety

It is believed that benzodiazepines reduce the activity of nerves in the central nervous system, enhancing the effects of GABA by opening GABA activated chloride channels and allowing chloride ions to enter the neuron, making it negatively charged and resistant to excitation.

Benzodiazepines

Benzodiazepams are most used for:

- Sedative-hypnotics for sleep
- Anesthesia
- Anxiety reduction
- Panic disorders
- Prevention/treatment of seizures
- Alcohol withdrawal
- Muscle relaxant

They have largely replaced barbiturates in the treatment of anxiety because benzos are much safer and more effective.

They are also the most widely used anxiolytic* drugs.



*Anxiolytic – drug used to relieve anxiety



TOP 10 DRUGS

CLONAZEPAM

Brand Name: Klonopin



TOP 10 DRUGS

LORAZEPAM

Brand Name: Ativan



Benzodiazepines

Pharmacology

science of drug action on biological systems

Clonazepam

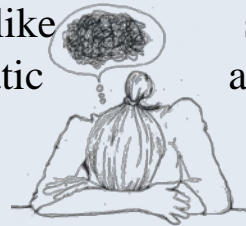
Known as a anxiolytic*, anticonvulsant & antiepileptic drug

Also, known to be long-acting agents with durations of action of 1-3 days

The onset of action usually occurs within 20-60 minutes.

Primarily used for treating panic disorders and preventing certain types of seizures

It can be used for treating other disorders like social phobia, mania and post-traumatic stress disorder.



Benzodiazepines

*Anxiolytic – drug used to relieve anxiety

Lorazepam

Known as a anxiolytic* and anticonvulsant drug and mild tranquilizer

Also, known to be intermediate-acting agents with durations of action of 11-20 hours

The onset of action usually occurs within 20-60 minutes.

Mostly used to relieve anxiety

It can also be used to treat irritable bowel syndrome, epilepsy, insomnia, nausea and vomiting from cancer treatments & control agitation caused by alcohol withdrawal.



Side Effects - Clonazepam

Common Side Effects:

- Upper respiratory congestion/infection
- Ataxia (type of clumsiness)
- Loss of balance/coordination
- Muscle weakness
- Frequent urination
- Drooling or dry mouth
- Memory loss
- Depression
- Loss of interest in sex
- Blurred vision
- Drowsiness/Dizziness
- Behavioral changes
- Slurred speech
- Loss of appetite, nausea, diarrhea & constipation
- Insomnia
- Weight changes/Anorexia



Severe Side Effects:

- Thoughts & attempts of suicide/dying
- New/Worsened seizures
- Easy bruising or bleeding
- Painful urination
- Unusual/involuntary eye movements
- Weak/shallow breathing
- Unusual risk-taking behavior (no fear of danger)
- Confusion/hallucinations
- Worsening depression
- Increase in mania
- Severe rash/hives
- Swelling of face, lips or tongue
- Acting aggressive, being angry or violent
- Other unusual behavior/moods



If any of these severe side effects are seen, call doctor immediately!

Benzodiazepines



Side Effects - Lorazepam

Common Side Effects

- Low blood pressure
- Blurred vision
- Skin rash
- Nausea/vomiting
- Insomnia
- Amnesia
- Sedation
- Dizziness
- Drowsiness
- Weakness
- Unsteadiness & Loss of coordination
- Appetite changes



Severe Side Effects

- Worsening/unmasking preexisting depression
- Respiratory depression (difficulty breathing)
- Liver dysfunction
- Anaphylactic (Severe allergic) reactions
- Swelling of face/throat
- Jaundice (yellowing of skin/eyes)
- Thoughts of suicide/harm
- Changes in mental state
- Hostility, agitation, hyperactivity
- Hallucinations
- Fainting

If any of these severe side effects are seen, call doctor immediately!



Associated Risks

Clonazepam

- Risk of dangerous & life-threatening drug dependence/addiction
- Increased risk of suicidal thoughts/actions
- Increased incidence or precipitate the onset of generalized tonic-clonic seizures (occurs with those who have several types of seizure disorders)
- Risk of abrupt withdrawal – may precipitate status epilepticus*
- Liver damage
- Impaired motor function
- Psychosis

*status epilepticus - a dangerous condition in which epileptic seizures follow one another without recovery of consciousness between them.

Lorazepam

- Risk of dangerous & life-threatening drug dependence/addiction
- Glaucoma (group of eye diseases that cause blindness)
- Sleep apnea (sleep disorder where breathing constantly stops)
- Increase in risk for gastrointestinal disturbances
- Respiratory suppression/failure

Benzodiazepines



Contraindications

A specific situation in which a drug, procedure, or surgery should not be used because it may be harmful to the patient.

Clonazepam

Clonazepam should not be used in patients with:

- history of sensitivity to benzodiazepines
- significant liver disease
- acute narrow angle glaucoma * but may be used in patients with open angle glaucoma who are receiving therapy
- history of substance abuse

*acute narrow angle glaucoma – condition where pressure inside of eye becomes too high

Lorazepam

Lorazepam should not be used in patients with:

- hypersensitivity to benzodiazepines
- acute narrow angle glaucoma
- sleep apnea syndrome
- severe respiratory insufficiency (except in those patients requiring relief of anxiety or diminished recall of events while being mechanically ventilated)
- use of Ativan Injection within an artery as inadvertent intra-arterial injection may produce arteriospasm resulting in gangrene which may require amputation
- history of substance abuse

Benzodiazepines



Pregnancy Risks

Clonazepam

Assumed to be capable of causing an increased risk of congenital abnormalities when administered to a pregnant woman during the first trimester.

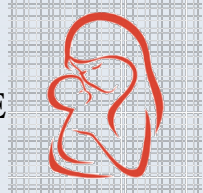
The possibility that a woman of childbearing potential may be pregnant at the time of institution of therapy should be considered.

If this drug is used during pregnancy or if the patient becomes pregnant while taking this drug, the patient should be informed of the potential hazard to the fetus.

Mothers receiving Clonazepam should not breast-feed their infants.

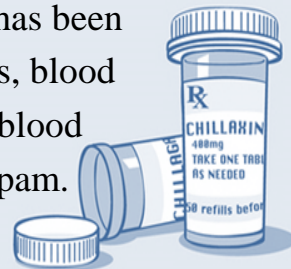
Lorazepam

ATIVAN MAY CAUSE FETAL DAMAGE
WHEN ADMINISTERED TO
PREGNANT WOMEN.



Ativan Injection should not be used during pregnancy except in serious or life-threatening conditions where safer drugs cannot be used or are ineffective. Status epilepticus may represent such a serious and life-threatening condition.

An increased risk of congenital malformations associated with the use of minor tranquilizers during the first trimester of pregnancy has been suggested in several studies. In humans, blood levels obtained from umbilical cord blood indicate placental transfer of lorazepam.



Potential Dangers

Clonazepam

Alcohol:

- Drinking alcohol may increase the effects of alcohol such as drowsiness, dizziness & sleepiness.

Interference with Cognitive & Motor Performance

- Individuals are cautioned against engaging in hazardous occupations requiring mental alertness such as driving or operating machinery.
- Accidental falls are common in elderly patients. Use caution to avoid falling or accidental injury.

Addiction/Abuse:

- Clonazepam is addictive. A person can form a physical dependence on the drug in as little as two weeks. Do not take this medication for longer than 9 weeks without your doctor's advice.
- Clonazepam may be used for long-term purposes **IF** *benefits outweigh the risks!*

Depressants/Other drugs

- Do not take CNS-depressant drugs or other drugs that will make you sleepy or dizzy while taking Clonazepam until you contact your healthcare provider. They can worsen symptoms such as dizziness and drowsiness.

Lorazepam

Alcohol:

- Drinking alcohol may increase the effects of alcohol such as drowsiness, dizziness & sleepiness.

Interference with Cognitive & Motor Performance

- Individuals are cautioned against engaging in hazardous occupations requiring mental alertness such as driving or operating machinery.
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Addiction/Abuse:

- Lorazepam is addictive. A person can form a physical dependence on the drug in as little as two weeks. Do not take this medication for longer than 9 weeks without your doctor's advice.
- Lorazepam may be used for long-term purposes **IF** *benefits outweigh the risks!*

Depressants/Other drugs

- Avoid using other medications that make you sleepy. They can add to sleepiness caused by lorazepam.



Potential Dangers continued

Other prescriptions: (Some MEDS MAY INTERACT with clonazepam!)

There are over 852 drugs (4828 brand and generic names) that are known to interact with clonazepam.

Always be cautious with drug interactions and always remind doctors of the client's use of clonazepam.

Listed below is a link to the site that has all medications that interact with clonazepam



<http://www.drugs.com/drug-interactions/clonazepam.html>

NOTE: Some drugs have multiple combinations, such as acetaminophen and hydrozine, with clonazepam. Please be aware of the combos that clonazepam can interact with.

Benzodiazepines



Common Meds. among APS clients. for Clonazepam

<u>Severity</u>		<u>Risks</u>
<u>High</u> (11 meds)	<u>Moderate</u> (744 meds)	
<ul style="list-style-type: none"> • Olanzapine (Zyrtec) • Levomethadyl Acetate (Orlaam) 	<ul style="list-style-type: none"> • Guanfacine (Intuniv) • Lisinopril 	<p>Can cause low blood pressure, shallow breathing, weak pulse, muscle weakness, drowsiness, dizziness & slurred speech</p>
<ul style="list-style-type: none"> • Acetaminophen/ Propoxyphene (Trycet) • Propoxyphene (Darvon) 	<ul style="list-style-type: none"> • Abilify (Aripiprazole) • Duloxetine (Cymbalta) • Lamotrigine (Lamictal) • Escitalopram (Lexapro) • Quetiapine (Seroquel) • Risperidone (Risperdal) 	<p>Increase side effects such as dizziness, drowsiness, confusion, difficulty concentrating and other nervous system or mental effects</p>
<ul style="list-style-type: none"> • Droperidol (Inapsine & Innovar) 		<p>Increase risk of an irregular heart rhythm that may be serious/life-threatening</p>
<ul style="list-style-type: none"> • Buprenorphine (Butrans & Buprenex) 		<p>Causes central nervous depression – leading to respiratory distress, coma or death</p>
	<ul style="list-style-type: none"> • Omeprazole • Fluvoxamine (Luvox) 	<p>Increase effects of clonazepam</p>

Benzodiazepines



Potential Dangers continued

Other prescriptions: (Some MEDS MAY INTERACT with lorazepam!)

There are over 772 drugs (4524 brand and generic names) that are known to interact with lorazepam.

Always be cautious with drug interactions and always remind doctors of the client's use of lorazepam.

Listed below is a link to the site that has all medications that interact with lorazepam



<http://www.drugs.com/drug-interactions/lorazepam.html>

NOTE: Some drugs have multiple combinations, such as acetaminophen and hydrozine, with lorazepam. Please be aware of the combos that lorazepam can interact with.

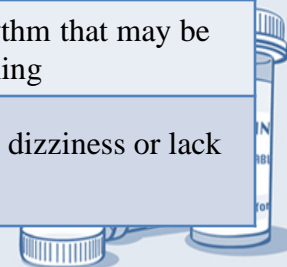
Benzodiazepines



Common Meds, among APS clients, for Lorazepam

Severity		Risks
<u>High</u> (12 meds)	<u>Moderate</u> (663 meds)	
<ul style="list-style-type: none"> •Olanzapine (Zyprexa) •Fluxoteine/Olanzapine (Symbax) •Levomethadyl Acetate 	<ul style="list-style-type: none"> •Clonidine •Tamsulosin (Flomax) •Hydrochlorothiazide 	Increase side effects such as low blood pressure, shallow breathing, weak pulse, muscle weakness, drowsiness, dizziness and slurred speech
<ul style="list-style-type: none"> •Clozapine (Zaponex, Denzapine, FlazaClo& Versacloz) 		Increases effects of both medications
<ul style="list-style-type: none"> •Sodium Oxybate (Xyrem) •Buprenorphine (Butrans) 		Increase risk of respiratory depression, low blood pressure, fainting, coma and death
<ul style="list-style-type: none"> •Propoxyphene (<ul style="list-style-type: none"> •Duloxetine (Cymbalta) •Escitalopram (Lexapro) •Pregabalin (Lyrica) •Aripiprazole (Abilify) 	Increase side effects such as dizziness, drowsiness, confusion, difficulty concentrating and other nervous system or mental effects
<ul style="list-style-type: none"> •Droperidol (Inapsine) 		Increase risk of an irregular heart rhythm that may be serious and life-threatening
<ul style="list-style-type: none"> •Quetiapine (Seroquel) 		Causes excessive sedation, confusion, dizziness or lack of coordination

Benzodiazepines



Laboratory Monitoring

Clonazepam

Lab tests, including liver function, complete blood cell counts, and electrocardiograms, may be performed while you use Klonopin. These tests may be used to monitor your condition or check for side effects.

Carry an ID card at all times that says you take Klonopin if it is used for seizures.

Lorazepam

Lab tests, including liver function and complete blood counts, may be performed while you use Ativan. These tests may be used to monitor your condition or check for side effects.

Benzodiazepines



(Self) Administration Instructions - Clonazepam

Take clonazepam exactly as prescribed by your doctor. Do not take in larger or smaller amounts or for longer than recommended. Follow the directions on your prescription label.

This medication comes in regular-release & orally disintegrating tablet form (wafer) and is taken usually 1-3 times a day, with or without food.

Regular-release tablets should be taken with water & swallowed whole!

Orally disintegrating tablets (wafers) are placed into the mouth & dissolve

- Do not open pouch until you are ready to take clonazepam.
- After opening the pouch, peel back the foil on the blister pack. (Do not push the wafer through the foil!)
- After opening the blister pack, with dry hands, take the tablet and place it in your mouth.
- The tablet will melt quickly.

Benzodiazepines



(Self) Administration Instructions - Lorazepam

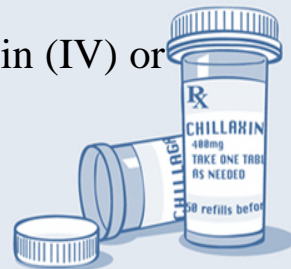
Take lorazepam exactly as it was prescribed for you. Follow the directions on your prescription label.

Do not take the medication in larger amounts, or take it for longer than recommended by your doctor.

This medication comes in tablet or oral solution forms & can be taken 1-3 times per day, with or without food.

The oral solution comes with a specially marked dropper for measuring the dose. Ask your pharmacist to show you how to use the dropper. Dilute the concentration in 1 ounce (30 milliliters) or more of water, juice or carbonated beverages just before taking it. It also may be mixed with applesauce or pudding just before taking the dose.

This medication is also available in an injectable form to be given directly into a vein (IV) or muscle (IM) by a healthcare professional.



Dosage

Clonazepam

Your doctor may occasionally change your dose to make sure you get the best results.

The dose your doctor recommends may be based on the following:

the condition being treated
other medical conditions you have
other medications you are taking
how you respond to this medication
your weight
your height
your age
your gender

The recommended dose for adults with seizure disorders should not exceed 1.5 mg/day divided into 3 doses. Maximum recommended daily dose is 20 mg.

In order to minimize drowsiness, the starting dose for infants and children (up to 10 years of age or 30 kg of body weight) should be between 0.01 and 0.03 mg/kg/day but not to exceed 0.05 mg/kg/day given in 2 or 3 divided doses.

Whenever possible, the daily dose should be divided into 3 equal doses.

If doses are not equally divided, the largest dose should be given before going to bed.

Lorazepam

Your doctor may occasionally change your dose to make sure you get the best results from this medication.

Oral Forms (oral solution and tablets):

The usual range is 2 to 6 mg every day taken in divided doses, but the daily dosage may vary from 1 to 10 mg/day.

The dosage of lorazepam should be increased gradually when needed to help avoid adverse effects.

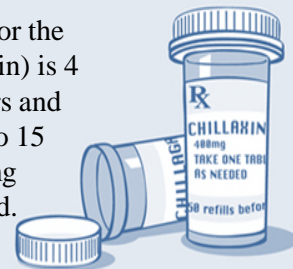
The dosage of lorazepam should be decreased gradually when appropriate to help avoid adverse effects during a withdrawal period.

In general, lorazepam should be used for short periods only (2 to 4 weeks). Your doctor will want to determine the need for continued therapy after this time period.

Injection:

Status epilepticus

The recommended dose of lorazepam injection for the treatment given as an IV injection (through the vein) is 4 mg given slowly (2 mg/min) for patients 18 years and older. If seizures continue or recur after a 10- to 15 minute observation period, an additional 4 mg intravenous dose may be slowly administered.



Management & Planning - Clonazepam

Clonazepam is a federally controlled substance (C-IV) because it can be abused or lead to dependence.

Keep track of the amount of medicine used from each new bottle. Clonazepam is a drug of abuse and you should be aware if anyone is using your medicine improperly or without a prescription.

Miss a dose? Call a pharmacist or doctor.

Overdose? Seek emergency medical attention or call the Poison Help line
@ 1-800-222-1222

Changing dose? Consult with a doctor and follow your doctor's instructions about tapering your dose.

Keep clonazepam in a safe place to prevent misuse and abuse.

Store between 59°F to 86°F (15°C to 30°C).

Additional documents may be required since clonazepam is a controlled substance.



Management & Planning - Lorazepam

Benzodiazepines are drugs of abuse and you should be aware if any person in the household is using this medicine improperly or without a prescription.

It is extremely important that you keep track of how many pills have been used from each new bottle of this medicine.

Keep the medication in a secure place where others cannot get to it.

Tablets:

Keep tightly closed in container.

Dispense in a tight container.

Store tablets at room temperature.

Oral solution:

Store in a refrigerator at 2°-8°C (36°-46°F).

Protect from light

Discard opened bottle after 90 days.

Injection:

Store injection (for IM or IV) in a refrigerator. Protect injection from light.

Lorazepam should be used for only a short time. Do not take this medication for longer than 4 months without your doctor's advice.

Miss a dose? Call a pharmacist or doctor.

Overdose? Seek emergency medical attention or call the Poison Help line

@ 1-800-222-1222

Changing dose? Consult with a doctor and follow your doctor's instructions about tapering your dose.

Additional documents may be required since clonazepam is a controlled substance.

Benzodiazepines



Nonadherence & Withdrawal

Clonazepam

ABRUPT DISCONTINUATION SHOULD BE AVOIDED!

A recent study by the American Family Physician Journal noted that almost 80% of people who have issues with Klonopin abuse also abuse other drugs, particularly heroin. In fact, many heroin and cocaine users take Klonopin, or “K-pin” to counteract the jittery feelings that many street drugs can cause, mistakenly believing that Klonopin is safer than other street drugs.

The abrupt withdrawal of Clonazepam, particularly in those patients on long-term, high dose therapy, may precipitate status epilepticus.

Therefore, when discontinuing Clonazepam, gradual withdrawal is essential. While Clonazepam is being gradually withdrawn, the simultaneous substitution of another anticonvulsant may be indicated.

Lorazepam

ABRUPT DISCONTINUATION SHOULD BE AVOIDED!

Continuous long-term use of product is not recommended.

Withdrawal symptoms (e.g. rebound insomnia) can appear following cessation of recommended doses after as little as one week of therapy.

Abrupt termination of treatment may be accompanied by withdrawal symptoms such as depression, irritability, rebound phenomena, dysphoria, hypersensitivity to light and noise, tremors, etc.

Benzodiazepines



Diet/Exercise

Clonazepam

Food interactions: This medication does not interact with food.

Smoking: Tends to lower plasma levels. If you smoke, a higher dosage of clonazepam will most likely be needed than someone who does not smoke.

If you stop smoking, the body clonazepam level rises and you might need to reduce the dosage of clonazepam slowly over a week.

Smoking cessation: Increased sedation is possible and lower dosages may be needed.

Clonazepam affects cognitive and motor abilities. It can make it hard to focus and concentrate on the task or activity at hand. Be cautious.

Lorazepam

Food interactions: This medication does not interact with food.

Smoking: Tends to lower plasma levels. If you smoke, a higher dosage of lorazepam will most likely be needed than someone who does not smoke.

If you stop smoking, the body lorazepam level rises and you might need to reduce the dosage of lorazepam slowly over a week.

Smoking cessation: Increased sedation is possible and lower dosages may be needed.

Lorazepam affects cognitive and motor abilities. It can make it hard to focus and concentrate on the task or activity at hand. Be cautious.



CAUTION: BENZO ABUSE!

Street Names: Downers, Nerve Pills, Tranks



Benzodiazepines are commonly abused. This abuse is partially related to the toxic effects that they produce and also to their widespread availability. They can be chronically abused or, as seen more commonly in hospital emergency departments, intentionally or accidentally taken in overdose. Death and serious illness rarely result from benzodiazepine abuse alone; however, they are frequently taken with either alcohol or other medications. The combination of benzodiazepines and alcohol can be dangerous.

Benzodiazepines have also been used as a "date rape" drug because they can markedly impair and even abolish functions that normally allow a person to resist or even want to resist sexual aggression or assault. In recent years, the detection and conviction of people involved in this has increased dramatically. The drug is usually added to alcohol-containing drinks or even soft drinks in powder or liquid forms and can be hard to taste.

Benzodiazepines



Additional Resources

It is dangerous to try and purchase clonazepam and lorazepam on the Internet or from vendors outside of the United States.

Medications distributed from Internet sales may contain dangerous ingredients, or may not be distributed by a licensed pharmacy.

Samples of lorazepam purchased on the Internet have been found to contain haloperidol (Haldol), a potent antipsychotic drug with dangerous side effects.

For more information, contact the U.S. Food and Drug Administration (FDA) or visit www.fda.gov/buyonlineguide.

