

ACAMPROSATE

THERAPEUTICS

**Brands** • Campral  
*see index for additional brand names*

**Generic?** Not in U.S.



**Class**

- Alcohol dependence treatment

**Commonly Prescribed for**  
*(bold for FDA approved)*

- **Maintenance of alcohol abstinence**



**How the Drug Works**

- Theoretically reduces excitatory glutamate neurotransmission and increases inhibitory gamma-aminobutyric acid (GABA) neurotransmission
- Binds to and blocks certain glutamate receptors, including metabotropic glutamate receptors
- Because withdrawal of alcohol following chronic administration can lead to excessive glutamate activity and deficient GABA activity, acamprosate can act as “artificial alcohol” to mitigate these effects

**How Long Until It Works**

- Has demonstrated efficacy in trials lasting between 13 and 52 weeks

**If It Works**

- Increases abstinence from alcohol

**If It Doesn't Work**

- Evaluate for and address contributing factors
- Consider switching to another agent
- Consider augmenting with naltrexone



**Best Augmenting Combos for Partial Response or Treatment Resistance**

- Naltrexone
- Augmentation therapy may be more effective than monotherapy
- Augmentation with behavioral, educational, and/or supportive therapy in groups or as an individual is probably key to successful treatment

**Tests**

- None for healthy individuals

SIDE EFFECTS

**How Drug Causes Side Effects**

- Theoretically, behavioral side effects due to changes in neurotransmitter concentrations at receptors in parts of the brain and body other than those that cause therapeutic actions
- Gastrointestinal side effects may be related to large doses of a drug that is an amino acid derivative, increasing osmotic absorption in the GI tract

**Notable Side Effects**

- Diarrhea, nausea
- Anxiety, depression

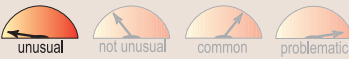


**Life-Threatening or Dangerous Side Effects**

- Suicidal ideation and behavior (suicidality)

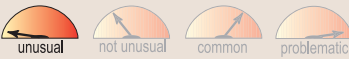
**Weight Gain**

- Reported but not expected



**Sedation**

- Reported but not expected



**What to Do About Side Effects**

- Wait
- Adjust dose
- If side effects persist, discontinue use

**Best Augmenting Agents for Side Effects**

- Dose reduction or switching to another agent may be more effective since most side effects cannot be improved with an augmenting agent

ACAMPROSATE (continued)

**DOSING AND USE**

**Usual Dosage Range**


- 666 mg three times daily

**Dosage Forms**

- Tablet 333 mg

**How To Dose**

- Patient should begin treatment as soon as possible after achieving abstinence
- Recommended dose is 666 mg three times daily; titration is not required

**Dosing Tips**

- Providing educational materials and counseling in combination with acamprosate treatment can increase the chances of success
- Patients should be advised to continue treatment even if relapse occurs and to disclose any renewed drinking
- Although absorption of acamprosate is not affected by food, it may aid adherence if patients who regularly eat three meals per day take each dose with a meal
- Adherence with three times daily dosing can be a problem; having patient focus on frequent oral dosing of drug rather than frequent drinking may be helpful in some patients

**Overdose**

- Limited available data; diarrhea

**Long-Term Use**

- Has been studied in trials up to one year

**Habit Forming**


- No

**How to Stop**

- Taper not necessary


**Pharmacokinetics**

- Terminal half-life 20–33 hours
- Excreted unchanged via the kidneys

**Drug Interactions**

- Does not inhibit hepatic enzymes, and thus is unlikely to affect plasma concentrations of drugs metabolized by those enzymes

- Is not hepatically metabolized and thus is unlikely to be affected by drugs that induce or inhibit hepatic enzymes
- Concomitant administration with naltrexone may increase plasma levels of acamprosate, but this does not appear to be clinically significant and dose adjustment is not recommended

**Other Warnings/Precautions**

- Monitor patients for emergence of depressed mood or suicidal ideation and behavior (suicidality)
- Use cautiously in individuals with known psychiatric illness

**Do Not Use**

- If patient has severe renal impairment
- If there is a proven allergy to acamprosate

**SPECIAL POPULATIONS**

**Renal Impairment**

- For moderate impairment, recommended dose is 333 mg three times daily
- Contraindicated in severe impairment

**Hepatic Impairment**


- Dose adjustment not generally necessary

**Cardiac Impairment**


- Limited available data

**Elderly**

- Some patients may tolerate lower doses better
- Consider monitoring renal function

**Children and Adolescents**

- Safety and efficacy have not been established

**Pregnancy**

- Risk Category C [some animal studies show adverse effects; no controlled studies in humans]
- Pregnant women needing to stop drinking may consider behavioral therapy before pharmacotherapy

(continued) **ACAMPROSATE**

- Not generally recommended for use during pregnancy, especially during first trimester

**Breast Feeding**

- Unknown if acamprosate is secreted in human breast milk, but all psychotropics assumed to be secreted in breast milk
- Recommended either to discontinue drug or bottle feed

**THE ART OF PSYCHOPHARMACOLOGY**

**Potential Advantages**


- Individuals who have recently abstained from alcohol
- For the chronic daily drinker

**Potential Disadvantages**


- Individuals who are not abstinent at time of treatment initiation
- For binge drinkers

**Primary Target Symptoms**

- Alcohol dependence

 **Pearls**

- Because acamprosate serves as “artificial alcohol,” it may be less effective in situations in which the individual has not yet abstained from alcohol or suffers a lapse
- Thus acamprosate may be a preferred treatment if the goal is complete abstinence, but may not be preferred if the goal is reduced-risk drinking



**Suggested Reading**

Anton RF, O'Malley SS, Ciraulo DA et al. Combined pharmacotherapies and behavioral interventions for alcohol dependence: the COMBINE study: a randomized controlled trial. JAMA 2006;295(17):2003–17.

Kranzler HR, Gage A. Acamprosate efficacy in alcohol-dependent patients: summary of results from three pivotal trials. Am J Addictions 2008;17:70–6.

Rosner S, Leucht S, Leherer P, Soyka M. Acamprosate supports abstinence, naltrexone prevents excessive drinking: evidence from a met-analysis with unreported outcomes. J Psychopharmacol 2008;22:11–23.

# ALPRAZOLAM

## THERAPEUTICS

**Brands** • Xanax, Xanax XR  
*see index for additional brand names*

**Generic?** Yes



### Class

- Benzodiazepine (anxiolytic)

**Commonly Prescribed for**  
*(bold for FDA approved)*

- **Generalized anxiety disorder (IR)**
- **Panic disorder (IR and XR)**
- Other anxiety disorders
- Anxiety associated with depression
- Premenstrual dysphoric disorder
- Irritable bowel syndrome and other somatic symptoms associated with anxiety disorders
- Insomnia
- Acute mania (adjunctive)
- Acute psychosis (adjunctive)



### How the Drug Works

- Binds to benzodiazepine receptors at the GABA-A ligand-gated chloride channel complex
- Enhances the inhibitory effects of GABA
- Boosts chloride conductance through GABA-regulated channels
- Inhibits neuronal activity presumably in amygdala-centered fear circuits to provide therapeutic benefits in anxiety disorders

### How Long Until It Works

- Some immediate relief with first dosing is common; can take several weeks with daily dosing for maximal therapeutic benefit

### If It Works

- For short-term symptoms of anxiety – after a few weeks, discontinue use or use on an “as-needed” basis
- For chronic anxiety disorders, the goal of treatment is complete remission of symptoms as well as prevention of future relapses
- For chronic anxiety disorders, treatment most often reduces or even eliminates symptoms, but not a cure since symptoms can recur after medicine stopped

- For long-term symptoms of anxiety, consider switching to an SSRI or SNRI for long-term maintenance
- If long-term maintenance with a benzodiazepine is necessary, continue treatment for 6 months after symptoms resolve, and then taper dose slowly
- If symptoms reemerge, consider treatment with an SSRI or SNRI, or consider restarting the benzodiazepine; sometimes benzodiazepines have to be used in combination with SSRIs or SNRIs for best results

### If It Doesn't Work

- Consider switching to another agent or adding an appropriate augmenting agent
- Consider psychotherapy, especially cognitive behavioral psychotherapy
- Consider presence of concomitant substance abuse
- Consider presence of alprazolam abuse
- Consider another diagnosis, such as a comorbid medical condition



### Best Augmenting Combos for Partial Response or Treatment Resistance

- Benzodiazepines are frequently used as augmenting agents for antipsychotics and mood stabilizers in the treatment of psychotic and bipolar disorders
- Benzodiazepines are frequently used as augmenting agents for SSRIs and SNRIs in the treatment of anxiety disorders
- Not generally rational to combine with other benzodiazepines
- Caution if using as an anxiolytic concomitantly with other sedative hypnotics for sleep

### Tests

- In patients with seizure disorders, concomitant medical illness, and/or those with multiple concomitant long-term medications, periodic liver tests and blood counts may be prudent

## SIDE EFFECTS

### How Drug Causes Side Effects

- Same mechanism for side effects as for therapeutic effects – namely due to

## ALPRAZOLAM (continued)

excessive actions at benzodiazepine receptors

- Long-term adaptations in benzodiazepine receptors may explain the development of dependence, tolerance, and withdrawal
- Side effects are generally immediate, but immediate side effects often disappear in time

### Notable Side Effects

- \* Sedation, fatigue, depression
- \* Dizziness, ataxia, slurred speech, weakness
- \* Forgetfulness, confusion
- \* Hyperexcitability, nervousness
- Rare hallucinations, mania
- Rare hypotension
- Hypersalivation, dry mouth



### Life-Threatening or Dangerous Side Effects

- Respiratory depression, especially when taken with CNS depressants in overdose
- Rare hepatic dysfunction, renal dysfunction, blood dyscrasias

### Weight Gain



- Reported but not expected

### Sedation



- Occurs in significant minority
- Especially at initiation of treatment or when dose increases
- Tolerance often develops over time

### What to Do About Side Effects

- Wait
- Wait
- Wait
- Lower the dose
- Switch to alprazolam XR
- Take largest dose at bedtime to avoid sedative effects during the day
- Switch to another agent
- Administer flumazenil if side effects are severe or life-threatening

### Best Augmenting Agents for Side Effects

- Many side effects cannot be improved with an augmenting agent

## DOSING AND USE

### Usual Dosage Range

- Anxiety: alprazolam IR: 1–4 mg/day
- Panic: alprazolam IR: 5–6 mg/day
- Panic: alprazolam XR: 3–6 mg/day

### Dosage Forms

- Alprazolam IR tablet 0.25 mg scored, 0.4 mg (Japan), 0.5 mg scored, 0.8 mg (Japan), 1 mg scored, 2 mg multiscored
- Alprazolam IR orally disintegrating tablet 0.25 mg, 0.5 mg, 1 mg, 2 mg
- Alprazolam IR solution, concentrate 1 mg/mL
- Alprazolam XR (extended-release) tablet 0.5 mg, 1 mg, 2 mg, 3 mg

### How To Dose

- For anxiety, alprazolam IR should be started at 0.75–1.5 mg/day divided into 3 doses; increase dose every 3–4 days until desired efficacy is reached; maximum dose generally 4 mg/day
- For panic, alprazolam IR should be started at 1.5 mg/day divided into 3 doses; increase 1 mg or less every 3–4 days until desired efficacy is reached, increasing by smaller amounts for dosage over 4 mg/day; may require as much as 10 mg/day for desired efficacy in difficult cases
- For panic, alprazolam XR should be started at 0.5–1 mg/day once daily in the morning; dose may be increased by 1 mg/day every 3–4 days until desired efficacy is reached; maximum dose generally 10 mg/day



### Dosing Tips

- Use lowest possible effective dose for the shortest possible period of time (a benzodiazepine-sparing strategy)
- Assess need for continued treatment regularly
- Risk of dependence may increase with dose and duration of treatment

- For interdose symptoms of anxiety, can either increase dose or maintain same total daily dose but divide into more frequent doses, or give as extended-release formulation
- Can also use an as-needed occasional “top up” dose for interdose anxiety
- Because panic disorder can require doses higher than 4 mg/day, the risk of dependence may be greater in these patients
- Some severely ill patients may require 8 mg/day or more
- Extended-release formulation needs to be taken only once or twice daily
- Do not break or chew XR tablets, as this will alter controlled-release properties
- Frequency of dosing in practice is often greater than predicted from half-life, as duration of biological activity is often shorter than pharmacokinetic terminal half-life
- Alprazolam and alprazolam XR generally dosed about one tenth the dosage of diazepam
- \* Alprazolam and alprazolam XR generally dosed about twice the dosage of clonazepam

### Overdose

- Fatalities have been reported both in monotherapy and in conjunction with alcohol; sedation, confusion, poor coordination, diminished reflexes, coma

### Long-Term Use

- Risk of dependence, particularly for treatment periods longer than 12 weeks and especially in patients with past or current polysubstance abuse

### Habit Forming

- Alprazolam is a Schedule IV drug
- Patients may develop dependence and/or tolerance with long-term use

### How to Stop

- Seizures may rarely occur on withdrawal, especially if withdrawal is abrupt; greater risk for doses above 4 mg and in those with additional risks for seizures, including those with a history of seizures
- Taper by 0.5 mg every 3 days to reduce chances of withdrawal effects

- For difficult to taper cases, consider reducing dose much more slowly after reaching 3 mg/day, perhaps by as little as 0.25 mg per week or less
- For other patients with severe problems discontinuing a benzodiazepine, dosing may need to be tapered over many months (i.e., reduce dose by 1% every 3 days by crushing tablet and suspending or dissolving in 100 mL of fruit juice and then disposing of 1 mL while drinking the rest; 3–7 days later, dispose of 2 mL, and so on). This is both a form of very slow biological tapering and a form of behavioral desensitization
- Be sure to differentiate reemergence of symptoms requiring reinstitution of treatment from withdrawal symptoms
- Benzodiazepine-dependent anxiety patients and insulin-dependent diabetics are not addicted to their medications. When benzodiazepine-dependent patients stop their medication, disease symptoms can reemerge or can worsen (rebound), and/or withdrawal symptoms can emerge

### Pharmacokinetics

- Metabolized by CYP450 3A4
- Inactive metabolites
- Elimination half-life 12–15 hours



### Drug Interactions

- Increased depressive effects when taken with other CNS depressants
- Inhibitors of CYP450 3A, such as nefazodone, fluvoxamine, fluoxetine, and even grapefruit juice, may decrease clearance of alprazolam and thereby raise alprazolam plasma levels and enhance sedative side effects; alprazolam dose may need to be lowered
- Thus, azole antifungal agents (such as ketoconazole and itraconazole), macrolide antibiotics, and protease inhibitors may also raise alprazolam plasma levels
- Inducers of CYP450 3A, such as carbamazepine, may increase clearance of alprazolam and lower alprazolam plasma levels and possibly reduce therapeutic effects

## ALPRAZOLAM (continued)



### Other Warnings/ Precautions

- Dosage changes should be made in collaboration with prescriber
- Use with caution in patients with pulmonary disease; rare reports of death after initiation of benzodiazepines in patients with severe pulmonary impairment
- History of drug or alcohol abuse often creates greater risk for dependency
- Hypomania and mania have occurred in depressed patients taking alprazolam
- Use only with extreme caution if patient has obstructive sleep apnea
- Some depressed patients may experience a worsening of suicidal ideation
- Some patients may exhibit abnormal thinking or behavioral changes similar to those caused by other CNS depressants (i.e., either depressant actions or disinhibiting actions)

### Do Not Use

- If patient has narrow angle-closure glaucoma
- If patient is taking ketoconazole or itraconazole (azole antifungal agents)
- If there is a proven allergy to alprazolam or any benzodiazepine

## SPECIAL POPULATIONS

### Renal Impairment

- Drug should be used with caution

### Hepatic Impairment

- Should begin with lower starting dose (0.5–0.75 mg/day in 2 or 3 divided doses)

### Cardiac Impairment

- Benzodiazepines have been used to treat anxiety associated with acute myocardial infarction

### Elderly

- Should begin with lower starting dose (0.5–0.75 mg/day in 2 or 3 divided doses) and be monitored closely



### Children and Adolescents

- Safety and efficacy not established but often used, especially short-term and at the lower end of the dosing scale

- Long-term effects of alprazolam in children/adolescents are unknown
- Should generally receive lower doses and be more closely monitored



### Pregnancy

- Risk Category D [positive evidence of risk to human fetus; potential benefits may still justify its use during pregnancy]
- Possible increased risk of birth defects when benzodiazepines taken during pregnancy
- Because of the potential risks, alprazolam is not generally recommended as treatment for anxiety during pregnancy, especially during the first trimester
- Drug should be tapered if discontinued
- Infants whose mothers received a benzodiazepine late in pregnancy may experience withdrawal effects
- Neonatal flaccidity has been reported in infants whose mothers took a benzodiazepine during pregnancy
- Seizures, even mild seizures, may cause harm to the embryo/fetus

### Breast Feeding

- Some drug is found in mother's breast milk
- ✱ Recommended either to discontinue drug or bottle feed
- Effects on infant have been observed and include feeding difficulties, sedation, and weight loss

## THE ART OF PSYCHOPHARMACOLOGY

### Potential Advantages

- Rapid onset of action
- Less sedation than some other benzodiazepines
- Availability of an XR formulation with longer duration of action

### Potential Disadvantages

- Euphoria may lead to abuse
- Abuse especially risky in past or present substance abusers

### Primary Target Symptoms

- Panic attacks
- Anxiety

**Pearls**

- \* One of the most popular benzodiazepines for anxiety, especially among primary care physicians and psychiatrists
- Is a very useful adjunct to SSRIs and SNRIs in the treatment of numerous anxiety disorders
- Not effective for treating psychosis as a monotherapy, but can be used as an adjunct to antipsychotics
- Not effective for treating bipolar disorder as a monotherapy, but can be used as an adjunct to mood stabilizers and antipsychotics
- May both cause depression and treat depression in different patients
- Risk of seizure is greatest during the first 3 days after discontinuation of alprazolam, especially in those with prior seizures, head injuries, or withdrawal from drugs of abuse
- Clinical duration of action may be shorter than plasma half-life, leading to dosing more frequently than 2–3 times daily in some patients, especially for immediate-release alprazolam
- Adding fluvoxamine, fluoxetine, or nefazodone can increase alprazolam levels and make the patient very sleepy unless the alprazolam dose is lowered by half or more
- When using to treat insomnia, remember that insomnia may be a symptom of some

other primary disorder itself, and thus warrant evaluation for comorbid psychiatric and/or medical conditions

- \* Alprazolam XR may be less sedating than immediate-release alprazolam
- \* Alprazolam XR may be dosed less frequently than immediate-release alprazolam, and lead to less interdose breakthrough symptoms and less “clock-watching” in anxious patients
- Slower rises in plasma drug levels for alprazolam XR have the potential to reduce euphoria/abuse liability, but this has not been proven
- Slower falls in plasma drug levels for alprazolam XR have the potential to facilitate drug discontinuation by reducing withdrawal symptoms, but this has not been proven
- \* Alprazolam XR generally has longer biological duration of action than clonazepam
- \* If clonazepam can be considered a “long-acting alprazolam-like anxiolytic,” then alprazolam XR can be considered “an even longer-acting clonazepam-like anxiolytic” with the potential of improved tolerability features in terms of less euphoria, abuse, dependence, and withdrawal problems, but this has not been proven

**Suggested Reading**

DeVane CL, Ware MR, Lydiard RB. Pharmacokinetics, pharmacodynamics, and treatment issues of benzodiazepines: alprazolam, adinazolam, and clonazepam. *Psychopharmacol Bull* 1991;27:463–73.

Greenblatt DJ, Wright CE. Clinical pharmacokinetics of alprazolam. Therapeutic implications. *Clin Pharmacokinet* 1993; 24:453–71.

Jonas JM, Cohon MS. A comparison of the safety and efficacy of alprazolam versus other agents in the treatment of anxiety, panic, and depression: a review of the literature. *J Clin Psychiatry* 1993;54 (Suppl):25–45.

Klein E. The role of extended-release benzodiazepines in the treatment of anxiety: a risk-benefit evaluation with a focus on extended-release alprazolam. *J Clin Psychiatry* 2002;63 (Suppl 14):27–33.

Speigel DA. Efficacy studies of alprazolam in panic disorder. *Psychopharmacol Bull* 1998; 34:191–95.

# AMISULPRIDE

## THERAPEUTICS

**Brands** • Solian  
*see index for additional brand names*

**Generic?** No



### Class

- Atypical antipsychotic (benzamide; possibly a dopamine stabilizer and dopamine partial agonist)

**Commonly Prescribed for**  
*(bold for FDA approved)*

- Schizophrenia, acute and chronic (outside of U.S., especially Europe)
- Dysthymia



### How the Drug Works

- Theoretically blocks presynaptic dopamine 2 receptors at low doses
- Theoretically blocks postsynaptic dopamine 2 receptors at higher doses
- \* May be a partial agonist at dopamine 2 receptors, which would theoretically reduce dopamine output when dopamine concentrations are high and increase dopamine output when dopamine concentrations are low
- Blocks dopamine 3 receptors, which may contribute to its clinical actions
- \* Unlike other atypical antipsychotics, amisulpride does not have potent actions at serotonin receptors

### How Long Until It Works

- Psychotic symptoms can improve within 1 week, but it may take several weeks for full effect on behavior as well as on cognition and affective stabilization
- Classically recommended to wait at least 4–6 weeks to determine efficacy of drug, but in practice some patients require up to 16–20 weeks to show a good response, especially on cognitive symptoms

### If It Works

- Most often reduces positive symptoms in schizophrenia but does not eliminate them
- Can improve negative symptoms, as well as aggressive, cognitive, and affective symptoms in schizophrenia

- Most schizophrenic patients do not have a total remission of symptoms but rather a reduction of symptoms by about a third
- Perhaps 5–15% of schizophrenic patients can experience an overall improvement of greater than 50–60%, especially when receiving stable treatment for more than a year
- Such patients are considered super-responders or “awakeners” since they may be well enough to be employed, live independently, and sustain long-term relationships
- Continue treatment until reaching a plateau of improvement
- After reaching a satisfactory plateau, continue treatment for at least a year after first episode of psychosis
- For second and subsequent episodes of psychosis, treatment may need to be indefinite
- Even for first episodes of psychosis, it may be preferable to continue treatment indefinitely to avoid subsequent episodes

### If It Doesn't Work

- Try one of the other first-line atypical antipsychotics (risperidone, olanzapine, quetiapine, ziprasidone, aripiprazole, paliperidone)
- If two or more antipsychotic monotherapies do not work, consider clozapine
- If no atypical antipsychotic is effective, consider higher doses or augmentation with valproate or lamotrigine
- Some patients may require treatment with a conventional antipsychotic
- Consider noncompliance and switch to another antipsychotic with fewer side effects or to an antipsychotic that can be given by depot injection
- Consider initiating rehabilitation and psychotherapy
- Consider presence of concomitant drug abuse



### Best Augmenting Combos for Partial Response or Treatment Resistance

- Valproic acid (valproate, divalproex, divalproex ER)
- Augmentation of amisulpride has not been systematically studied

## AMISULPRIDE (continued)

- Other mood-stabilizing anticonvulsants (carbamazepine, oxcarbazepine, lamotrigine)
- Lithium
- Benzodiazepines

### Tests

- \* Although risk of diabetes and dyslipidemia with amisulpride has not been systematically studied, monitoring as for all other atypical antipsychotics is suggested

### Before starting an atypical antipsychotic

- \* Weigh all patients and track BMI during treatment
- Get baseline personal and family history of diabetes, obesity, dyslipidemia, hypertension, and cardiovascular disease
- Get waistline circumference (at umbilicus), blood pressure, fasting plasma glucose, and fasting lipid profile
- Determine if patient is
  - overweight (BMI 25.0–29.9)
  - obese (BMI ≥30)
  - has pre-diabetes (fasting plasma glucose 100–25 mg/dL)
  - has diabetes (fasting plasma glucose >126 mg/dL)
  - has hypertension (BP >140/90 mm Hg)
  - has dyslipidemia (increased total cholesterol, LDL cholesterol, and triglycerides; decreased HDL cholesterol)
- Treat or refer such patients for treatment, including nutrition and weight management, physical activity counseling, smoking cessation, and medical management

### Monitoring after starting an atypical antipsychotic

- \* BMI monthly for 3 months, then quarterly
- Consider monitoring fasting triglycerides monthly for several months in patients at high risk for metabolic complications and when initiating or switching antipsychotics
- Blood pressure, fasting plasma glucose, fasting lipids within 3 months and then annually, but earlier and more frequently for patients with diabetes or who have gained >5% initial weight
- Treat or refer for treatment and consider switching to another atypical antipsychotic for patients who become overweight, obese, pre-diabetic, diabetic, hypertensive, or dyslipidemic while receiving an atypical antipsychotic

- \* Even in patients without known diabetes, be vigilant for the rare but life-threatening onset of diabetic ketoacidosis, which always requires immediate treatment by monitoring for the rapid onset of polyuria, polydipsia, weight loss, nausea, vomiting, dehydration, rapid respiration, weakness and clouding of sensorium, even coma
- EKGs may be useful for selected patients (e.g., those with personal or family history of QTc prolongation; cardiac arrhythmia; recent myocardial infarction; uncompensated heart failure; or taking agents that prolong QTc interval such as pimozide, thioridazine, selected antiarrhythmics, moxifloxacin, sparfloxacin, etc.)
- Patients at risk for electrolyte disturbances (e.g., patients on diuretic therapy) should have baseline and periodic serum potassium and magnesium measurements

## SIDE EFFECTS

### How Drug Causes Side Effects

- By blocking dopamine 2 receptors in the striatum, it can cause motor side effects, especially at high doses
- By blocking dopamine 2 receptors in the pituitary, it can cause elevations in prolactin
- Mechanism of weight gain and possible increased incidence of diabetes and dyslipidemia with atypical antipsychotics is unknown

### Notable Side Effects

- \* Extrapyramidal symptoms
- \* Galactorrhea, amenorrhea
- \* Atypical antipsychotics may increase the risk for diabetes and dyslipidemia, although the specific risks associated with amisulpride are unknown
- Insomnia, sedation, agitation, anxiety
- Constipation, weight gain
- Rare tardive dyskinesia



### Life-Threatening or Dangerous Side Effects

- Rare neuroleptic malignant syndrome
- Rare seizures
- Dose-dependent QTc prolongation