

Bipolar Mania

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THE STORY IN ONE SENTENCE

Mania is a medical emergency when the person cannot think clearly, acts dangerously, or loses touch with reality.

“Mania happens when dopamine (a brain chemical that drives energy and reward) floods the control centers, shuts down sleep and judgment, and makes the person feel unstoppable even as they race toward danger.”

Normal anatomy — the body's job

In a healthy brain, the prefrontal cortex (the front part that plans ahead, judges risk, and stops impulses) and the limbic system (deep emotional centers that generate feelings and drive) stay balanced through carefully controlled dopamine, serotonin (a calming messenger), and GABA (the brain's main brake chemical).

BODY'S JOB

These circuits regulate mood, the sleep-wake cycle, judgment, and how you see reality. When balanced, you sleep on a regular schedule, think step by step, make safe choices, and see the world accurately.

1. The hypothalamus (a small control center deep in the brain) tracks your sleep need by watching adenosine (a chemical that builds up the longer you are awake) and sends sleep signals when it is time to rest.
2. The prefrontal cortex receives ideas and urges from the limbic system, weighs the consequences, and decides which actions are safe before you act.
3. Dopamine pathways (the reward circuits) fire when you expect pleasure or reach a goal, giving you motivation without overwhelming judgment.
4. Serotonin and GABA (inhibitory messengers, meaning they act like brakes) slow thoughts and emotions so they stay in a manageable range.

5. Together, these systems keep mood stable, sleep regular, and behavior lined up with reality and safety.

What breaks

In mania, dopamine floods the reward and emotion circuits and the prefrontal cortex cannot stop it. The brakes fail. Sleep disappears because high dopamine overrides the sleep signal. Judgment vanishes because the planning center goes offline. Triggers include stopping mood stabilizers, using stimulants (cocaine, methamphetamine, high-dose caffeine), severe stress, or even seasonal changes—spring light shifts can flip the switch. Genetic vulnerability loads the gun; stress, drugs, or skipping medication pulls the trigger.

CLINICAL TERM

Dysregulation of dopaminergic signaling in the mesolimbic and mesocortical pathways (the brain circuits that process reward, motivation, and executive control) produces disinhibition (loss of normal behavioral brakes), hyperarousal (the brain stays locked in high alert), decreased need for sleep, and in severe cases psychotic symptoms (hallucinations or delusions) via excessive D2 receptor stimulation. Genetic polymorphisms (variations in genes that regulate neurotransmitter systems), psychosocial stressors, circadian disruption (disrupted sleep-wake rhythm), substance use, and medication nonadherence all amplify circuit dysfunction. The result is a positive-feedback loop: dopamine excess leads to sleep loss, which leads to more dopamine, which leads to worsening mania.

How the body compensates

Early in mania, the person feels fantastic—energized, confident, creative, needing little sleep—and does not see danger. Family, friends, and clinicians must understand that this elevated mood is unstable and can rapidly spiral into psychosis, violence, financial ruin, or medical crisis. Catching the episode before full-blown mania is the goal; once psychotic features appear, hospitalization is often required to prevent harm.

1. The brain's reward circuits fire intensely, flooding the person with euphoria (extreme happiness) and grandiosity (inflated belief in one's own power or importance). This feels real and wonderful, not like illness, so the person pushes back against treatment.
2. Sleep loss drives the mania through a vicious cycle: less sleep leads to more dopamine, which leads to more mania, which leads to even less sleep. Each night without rest speeds up the episode. Restoring sleep is the first clinical priority.

3. The person's judgment is offline but they feel smarter than ever. They make decisions—quit a job, buy a car, start a business, engage in risky sex—that feel genius in the moment but cause catastrophic consequences later.
4. Psychosis can emerge within days: command hallucinations (voices ordering harmful acts), paranoid delusions (false beliefs that others are plotting harm), or grandiose delusions (I am a prophet, I can fly). These are medical emergencies.
5. Other dangers include agitation and violence (especially if goals are blocked), reckless spending leading to financial ruin, hypersexuality causing relationship or legal harm, dehydration (the person forgets to drink) leading to lithium toxicity if on lithium, and post-episode depression with high suicide risk.
6. Always assess trajectory: Is the person escalating? Are they safe at home? Can they work with treatment? Early inpatient care prevents disasters.

Domino effect

1. Dopamine floods the mesolimbic reward pathway (the circuit running from the brain's dopamine factory to the reward center). — Genetic vulnerability (inherited variations in dopamine-regulating genes), major stress, sleep deprivation, stimulant use (cocaine, methamphetamine), or stopping mood stabilizers trigger excessive dopamine release that the prefrontal cortex cannot shut down. The system loses its normal off-switch.
2. Sleep drive disappears; the person needs only two to three hours per night or none at all and feels fully energized. — High dopamine blocks adenosine (the brain chemical that builds up to make you sleepy) and overrides the hypothalamus (the master sleep-wake regulator), so the brain never signals it is time to sleep. The person truly does not feel tired.
3. Pressured speech: talking is rapid, loud, hard to interrupt, and pours out in a continuous stream. — Dopamine speeds up thought generation and motor output (the signals that move your mouth and vocal cords). The prefrontal cortex normally pauses speech to organize ideas and listen; in mania that system is offline, so words flow without editing or turn-taking.
4. Flight of ideas: thoughts race and jump from topic to topic with loose or no logical connections. — The same dopamine surge speeds up associative thinking (how your brain links one idea to the next) but shuts down executive function (the ability to organize, sequence, and filter thoughts). Ideas scatter faster than the person can follow, and barely related links feel deep and meaningful.
5. Euphoria or irritability: mood is abnormally elevated (feeling on top of the world) or explosively angry. — Dopamine and other monoamines (chemical messengers including norepinephrine and serotonin) flood the limbic system, producing intense positive emotion. If a goal is blocked or someone disagrees, the same overactive circuit flips instantly to rage because the brakes are gone.

6. Risky behaviors: spending sprees, reckless driving, hypersexuality (abnormally increased sexual desire or activity), impulsive business deals, or aggressive confrontations. — The prefrontal cortex normally stops impulses by imagining future consequences. In mania that system is silent, so every urge feels urgent, brilliant, and consequence-free. The person acts on desires immediately without weighing danger or social cost.
7. Psychotic symptoms appear in severe mania: delusions (fixed false beliefs, such as I have special powers or the FBI is following me) or hallucinations (hearing voices, seeing things not present). — Extreme dopamine excess in the mesolimbic pathway disrupts reality testing (the brain's ability to tell real from false signals) and generates false sensory input, the same mechanism that drives psychosis in schizophrenia. The person loses the ability to recognize that these experiences are not real.
8. Crash risk: After days to weeks of mania, the brain exhausts its resources and mood plunges into severe depression, often with suicidal thoughts. — The manic surge drains neurotransmitter stores and throws receptors (the docking sites on brain cells that receive chemical signals) out of balance. The same circuits that were stuck in overdrive now cannot generate normal mood or energy, and the person faces the wreckage—financial, social, legal—left by manic decisions. Suicide risk is highest in this post-manic phase.

Symptoms · what the patient feels, and why

- Decreased need for sleep: High dopamine (a brain messenger that drives energy and alertness) blocks adenosine (the molecule that piles up during the day to make you sleepy) and shuts down the sleep switch in the hypothalamus (the brain's control center for sleep and wake). The person feels fully rested on 2–3 hours of sleep, or sometimes none at all.
- Pressured speech: Dopamine speeds up thought and movement commands from the motor cortex (the strip of brain that controls voluntary movement), while the prefrontal cortex (the brain's pause button at the front) goes offline. The person talks fast, loud, and nonstop—like a runaway train with no brakes.
- Racing thoughts or flight of ideas: Too much dopamine makes connections between ideas happen at high speed, but the dorsolateral prefrontal cortex (the part of the front brain that organizes and finishes one thought before jumping to the next) is disabled. Thoughts pile up, skip around, and scatter like a deck of cards spilling onto the floor.
- Euphoria or irritability: Dopamine and norepinephrine (a stimulating brain messenger) flood the nucleus accumbens and ventral tegmental area (the brain's main pleasure and reward centers deep inside). This creates extreme highs and a feeling that everything is amazing. When goals are blocked or someone says no, the same overcharged circuit flips to anger and irritability.

- **Grandiosity:** The prefrontal cortex (the brain's reality-checker at the front) loses its power to test beliefs against facts. Inflated ideas—like 'I am famous,' 'I have special powers,' or 'I can do anything'—feel absolutely true and unshakable, even when they are not.
- **Increased goal-directed activity or agitation:** The dopamine surge drives intense motivation and motor activity (movement drive) from the basal ganglia (clusters of nerve cells deep in the brain that control movement). The person starts many projects at once, cannot sit still, and may pace, fidget, or become physically aggressive—like an engine revving too high with no way to slow down.
- **Risky behavior (excessive spending, hypersexuality, substance use, reckless driving):** The ventromedial prefrontal cortex (the part of the front brain that weighs consequences before acting) is shut off, so impulses are not checked for danger. Every idea feels brilliant and urgent, leading to dangerous choices like maxing out credit cards, unsafe sex, drug binges, or speeding at 100 miles per hour.
- **Psychotic symptoms (delusions or hallucinations):** Extreme dopamine excess overwhelms the mesolimbic pathway (the dopamine highway that runs from the midbrain to deep emotional centers), creating false sensory signals (hearing or seeing things that are not there) and delusional beliefs (fixed false ideas like 'I am God' or 'The FBI is after me').
- **Distractibility:** The dorsolateral prefrontal cortex (the brain's focus filter at the front) cannot hold attention on one task. Every sight, sound, or passing thought grabs attention equally, making it impossible to finish anything—like trying to read a book while a hundred TVs play at full volume around you.

Focused exam

- **Decreased need for sleep — patient slept only 2 hours but feels completely rested and full of energy:** In mania, the brain's sleep center (the hypothalamus) and the body's natural day-night clock (circadian rhythm) stop working correctly. The person truly does not feel tired even with almost no sleep. This is the key feature that separates real mania from just feeling happy or excited, because normal excitement still leaves you tired if you skip sleep.
- **Pressured speech (talking fast, loud, hard to interrupt) and flight of ideas (jumping from topic to topic without finishing thoughts):** Mania speeds up the brain's speech areas and shuts off the normal brake that lets you pause and stay on one idea. This happens because dopamine (a brain messenger that controls thought speed, movement, and reward) is flooding the language and thinking parts of the brain, making them fire too fast. It shows the brain is running in overdrive.

- Elevated or irritable mood — patient feels on top of the world (euphoric) but gets angry or frustrated very quickly when challenged or told no: Mania breaks the brain's emotion control center (the prefrontal cortex, the front part of your brain that helps you think before you act). High mood plus quick anger leads to dangerous, impulsive choices like spending all your money, risky sex, reckless driving, or picking fights, which can ruin your life fast.
- Engagement in high-risk activities — out-of-control spending, much more sexual activity than usual (hypersexuality), reckless driving, or starting many big projects at once: Mania turns up the brain's reward system (the part that makes you crave pleasure, called the nucleus accumbens) while turning down the judgment center (prefrontal cortex, which normally warns you about consequences). This removes the normal brake on impulses, so the person does things that can lead to bankruptcy, losing a job, sexually transmitted infections, legal trouble, or destroyed relationships.
- Racing thoughts with many started projects but nothing finished — patient has dozens of ideas flying through their head and starts tasks constantly but cannot complete any of them: Too much dopamine in the thinking part of the brain (prefrontal cortex) makes thoughts race faster than the brain can organize them or focus on one thing. This scattered pattern is a core sign of the chemical imbalance driving the manic episode.
- Dilated pupils (bigger than normal pupils), sweating, fast heartbeat over 100 beats per minute (tachycardia), or shaking hands (tremor): These body signs come from the fight-or-flight system (sympathetic nervous system) turning on too high during severe mania. But these same signs also happen with stimulant drugs like cocaine or methamphetamine, so you must check for drug use right away because the treatment changes completely if drugs are involved.
- Psychotic features — hearing voices that are not there (auditory hallucinations), seeing things that are not there (visual hallucinations), or believing you have special powers, are famous, or are extremely rich when you are not (grandiose delusions): Severe mania can cause the brain's dopamine circuits (especially the mesolimbic pathway, which controls reward and perception) to go so far out of balance that the person loses touch with reality. Psychosis means the episode is very serious and needs antipsychotic medicine immediately to prevent harm.

Diagnostics · every test answers a question

- Thyroid-stimulating hormone (TSH) blood test → Is the thyroid gland overactive and mimicking or triggering mania?
- Urine drug screen (UDS) → Is the patient using stimulant drugs that can cause or worsen mania?

- Comprehensive metabolic panel (CMP) — blood test checking sodium, potassium, glucose, kidney function (creatinine), and liver enzymes → Are the kidneys and liver healthy enough to safely process mood medications, and are there metabolic problems affecting the brain?
- Complete blood count (CBC) with differential → Is there an infection or blood disorder that could trigger behavioral changes?
- Serum lithium level (if patient is already taking lithium) → Is the lithium dose in the safe and effective range, or is it too high or too low?
- Urine or serum pregnancy test (in all women of childbearing age, typically ages 12 to 50) → Is the patient pregnant, which changes which medications are safe?
- Electrocardiogram (ECG) if starting antipsychotic medication or lithium → Is the heart's electrical rhythm normal, or is there a hidden problem that certain mood medicines could make worse?
- Collateral history from family, friends, or prior medical records → Has the patient had mood episodes before, and is there family history of bipolar disorder or suicide?

Treatment logic

- Start an antipsychotic medication immediately — first-line choices include olanzapine, risperidone, quetiapine, or aripiprazole (oral or, if needed, intramuscular injection for severe agitation) → Antipsychotics block dopamine receptors (specifically the D2 type) in the brain's reward and perception circuits (mesolimbic and mesocortical pathways), which are firing too fast during mania. This slows down racing thoughts, pressured speech, agitation, and psychotic symptoms like hallucinations or delusions. You can see improvement within hours to a few days.
- Add a mood stabilizer — lithium or valproate (divalproex sodium) — within 24 to 48 hours of starting the antipsychotic → Lithium works inside brain cells to calm overactive signaling pathways (like inositol and glycogen synthase kinase-3) that control how excitable neurons are. Valproate boosts GABA (the brain's main calming chemical), which quiets abnormal electrical storms in mood-regulating brain areas like the limbic system (emotion control center). Both medicines stabilize mood over 1 to 2 weeks and reduce the chance of future manic or depressive episodes.
- Give a benzodiazepine — lorazepam or clonazepam — for severe agitation and insomnia (short-term use only, typically 3 to 7 days) → Benzodiazepines turn up GABA-A receptors, which are the brain's emergency brake. This quiets overactive neurons in the amygdala (fear and stress center) and cortex (thinking center), helping the person calm down and sleep. Sleep is critical because it helps reset the body's day-night clock (circadian rhythm), which is completely out of sync during mania.

- Admit the patient to an inpatient psychiatric unit if they are a danger to themselves or others, have no stable place to live or support system, or are so impulsive they cannot follow outpatient treatment → The hospital provides 24-hour monitoring to prevent suicide, violence, financial disaster (like emptying bank accounts), legal trouble (like arrests), or sexually transmitted infections. It also removes access to things that enable impulsive behavior (credit cards, car keys, drugs, alcohol) and makes sure the patient takes medications every day during the highest-risk window while waiting for medicines to work.
- Stop all antidepressant medications immediately if the patient is currently taking them (such as SSRIs, SNRIs, or tricyclics) → Antidepressants can flip the brain from depressed to manic by increasing serotonin or norepinephrine in circuits that are already overactive, making mania worse or causing rapid cycling (mood switching back and forth quickly). Stopping these medicines removes fuel from the fire.
- Arrange discharge planning that includes stable housing, substance use disorder treatment if needed, and outpatient psychotherapy (such as cognitive-behavioral therapy or family-focused therapy) → Homelessness and active drug or alcohol use turn on the body's chronic stress system (the hypothalamic-pituitary-adrenal axis, which releases cortisol and keeps the brain on high alert), which keeps mood circuits unstable and makes future manic or depressive episodes much more likely. Stable housing and stopping substance use remove these constant brain stressors. Therapy helps the patient recognize early warning signs of a new episode and build skills to manage stress without relapse.

Medications

Olanzapine · Second-generation antipsychotic (also called an atypical antipsychotic)

Olanzapine blocks dopamine D₂ receptors (tiny landing pads on brain cells where dopamine delivers its signal) in the brain's reward and emotion centers. When dopamine is too active in mania, thoughts race, judgment breaks down, and mood shoots sky-high. Blocking these receptors calms that overactivity. It also blocks serotonin 5-HT_{2A} receptors (docking sites for serotonin, another brain messenger), which helps smooth out mood swings and reduces irritability.

1. Olanzapine enters the bloodstream after you swallow the pill, then crosses into the brain.
2. It attaches to dopamine D₂ receptors (the main docking station for dopamine) and blocks them, so dopamine cannot land there and fire up the cell.
3. This reduces the overactive signaling in the reward circuit that drives racing thoughts, grandiose ideas (believing you have special powers or are incredibly important), and reckless behavior.
4. It also blocks serotonin 5-HT_{2A} receptors, which helps balance mood and reduce agitation.

5. Over days to weeks, the brain's chemical balance shifts: racing thoughts slow, sleep improves, and risky impulses ease.

SAFETY WATCH

Weight gain and increased appetite are very common—the drug makes you hungrier and slows your metabolism. · Blood sugar can rise (hyperglycemia, meaning too much sugar in the blood), sometimes leading to diabetes, so your doctor will check fasting blood sugar and hemoglobin A1c regularly. · Cholesterol and triglycerides (fats in the blood) often climb, raising heart-disease risk over time. · Sedation (feeling very sleepy or drowsy) is common, especially in the first few weeks. · Rare but serious: neuroleptic malignant syndrome (high fever, stiff muscles, confusion, fast heart rate)—go to the emergency room immediately if this happens. · Older adults with dementia should NOT use this drug; it raises the risk of stroke and death.

Risperidone · Second-generation antipsychotic (also called an atypical antipsychotic)

Risperidone blocks dopamine D₂ receptors (tiny landing pads on brain cells where dopamine delivers its 'speed up' signal) in the brain's emotion and reward centers. Too much dopamine activity in mania makes thoughts race, mood soar too high, and impulses dangerous. Blocking these receptors slows that runaway signaling. It also blocks serotonin 5-HT_{2A} receptors (docking sites for serotonin, a mood-steadying messenger), which helps stabilize mood and reduce irritability.

1. Risperidone enters the bloodstream after you swallow it or let the dissolving tablet melt in your mouth, then crosses into the brain.
2. It locks onto dopamine D₂ receptors and blocks them, so dopamine cannot activate the cell.
3. This reduces overactive signaling in the reward and emotion circuits, calming racing thoughts, grandiose beliefs (thinking you are far more powerful or important than you are), and reckless behavior.
4. It also blocks serotonin 5-HT_{2A} receptors, which balances mood and eases agitation.
5. Over several days, mania symptoms ease: sleep returns, impulsivity drops, and thinking clears.

SAFETY WATCH

Prolactin (a hormone that triggers milk production) often rises, which can cause breast enlargement or milk leak in both men and women, missed periods, and sexual problems. · Weight gain and increased appetite are common, though usually less than with olanzapine. · Blood sugar can rise, increasing diabetes risk—your doctor will monitor fasting glucose and A1c. · Movement side effects (tremor, stiffness, restlessness) are more common than with other second-generation drugs, especially at higher doses. · Sedation (feeling drowsy or sluggish) happens often, especially early on. · Rare but serious: neuroleptic malignant syndrome (high fever, muscle rigidity, confusion)—seek emergency care immediately. · Older adults with dementia should NOT use this drug; it raises stroke and death risk.

Quetiapine · Second-generation antipsychotic (also called an atypical antipsychotic)

Quetiapine blocks dopamine D₂ receptors (docking stations on brain cells that receive dopamine, a chemical messenger) in the brain's emotion and reward circuits. In mania, dopamine is overactive, driving racing thoughts, sky-high mood, and poor judgment. Blocking these receptors tamps down that runaway activity. Quetiapine also blocks histamine H₁ receptors (which keep you awake—the same chemical your body releases during allergies) and serotonin 5-HT_{2A} receptors (sites for serotonin, a mood-balancing messenger), helping restore sleep and smooth out mood.

1. Quetiapine enters the bloodstream after you swallow it, then crosses into the brain.
2. It attaches to dopamine D₂ receptors and blocks them, so dopamine cannot activate the cell.
3. This reduces overactive signaling in the reward circuit, calming racing thoughts, grandiose ideas (thinking you have special abilities or importance), and risky impulses.
4. It also blocks histamine H₁ receptors, which makes you sleepy and helps repair disrupted sleep.
5. It blocks serotonin 5-HT_{2A} receptors, which stabilizes mood and reduces irritability.
6. Over days to weeks, mania eases: sleep returns, energy normalizes, and impulsivity drops.

SAFETY WATCH

Sedation (feeling very drowsy) is extremely common, especially in the first few weeks—take it at bedtime. · Weight gain and increased appetite happen often. · Blood sugar can rise (hyperglycemia, meaning too much sugar in the blood), raising diabetes risk—your doctor will check fasting glucose and hemoglobin A1c regularly. · Cholesterol and triglycerides (fats in the blood) often increase. · Dizziness or lightheadedness when standing up (orthostatic low blood pressure (hypotension), meaning blood pressure drops when you stand) is common—stand up slowly. · Rare but serious: neuroleptic malignant syndrome (high fever, stiff muscles, confusion)—get emergency care immediately. · Older adults with dementia should NOT use this drug; it raises stroke and death risk.

Aripiprazole · Second-generation antipsychotic (also called an atypical antipsychotic)

Aripiprazole is a partial agonist at dopamine D₂ receptors (it sits on the receptor and turns it on just a little, not all the way). When dopamine is too high (like in mania), aripiprazole acts like a brake, blocking some of the overactive dopamine signal. When dopamine is too low, it gently nudges the receptor to keep some activity going. This balancing act calms mania without shutting dopamine down completely. It also partially activates serotonin 5-HT_{1A} receptors (which help stabilize mood) and blocks serotonin 5-HT_{2A} receptors (which reduces agitation).

1. Aripiprazole enters the bloodstream after you swallow it, then crosses into the brain.
2. It attaches to dopamine D₂ receptors and partially activates them (about 30% of full activity), which means it stabilizes dopamine signaling instead of blocking it completely.
3. When dopamine is overactive (as in mania), aripiprazole acts like a brake, preventing full dopamine firing and calming racing thoughts, grandiose ideas (believing you are far more special or powerful than you are), and risky behavior.
4. It also partially activates serotonin 5-HT_{1A} receptors, which helps steady mood and reduce anxiety.
5. It blocks serotonin 5-HT_{2A} receptors, which reduces irritability and agitation.
6. Over days to weeks, mania symptoms ease: mood stabilizes, impulsivity drops, and sleep improves.

SAFETY WATCH

Restlessness (akathisia, a feeling of inner tension and need to move) is very common, especially in the first few weeks—tell your doctor if this happens. · Weight gain is less common than with other antipsychotics, but still possible. · Blood sugar can rise, though the risk is lower than with olanzapine or quetiapine—your doctor will still monitor fasting glucose and A1c. · Nausea and stomach upset are common, especially when starting. · Insomnia (trouble falling or staying asleep) can occur. · Movement side effects (tremor, stiffness) are possible but less common than with older antipsychotics. · Rare but serious: neuroleptic malignant syndrome (high fever, stiff muscles, confusion)—get emergency care immediately. · Older adults with dementia should NOT use this drug; it raises stroke and death risk.

Lithium · Mood stabilizer

Lithium is a simple salt (like table salt, but a different element) that changes the way brain cells send signals to each other. It reduces overactivity in the brain circuits that control mood and impulse. Exactly how it works is not fully known, but it seems to calm the 'amplifier' inside brain cells (enzymes and signaling proteins that boost signals) so mood swings are less extreme. It also protects brain cells from damage over time by boosting growth factors (proteins that help cells survive and repair).

1. Lithium enters the bloodstream after you swallow it, then crosses into the brain and enters brain cells.
2. Inside the cells, it interferes with enzymes (tiny molecular machines) that amplify signals, turning down overactive pathways like inositol recycling and GSK-3 activity.
3. It reduces the release of excitatory neurotransmitters (chemicals like glutamate that speed up brain activity) and boosts the activity of inhibitory systems (like GABA, the brain's main calming chemical).
4. Over weeks, the brain's mood circuits stabilize: extreme highs flatten, impulsivity drops, and mood swings become less severe.
5. Lithium also increases brain-derived neurotrophic factor (BDNF, a protein that helps brain cells grow and survive), which may protect against future episodes.

SAFETY WATCH

Narrow therapeutic window: the safe dose is very close to the toxic dose, so blood levels must be checked regularly (target 0.6–1.2 mEq/L for maintenance, 0.8–1.2 for acute mania). · Kidney damage (chronic kidney disease) can develop over years—your doctor will monitor creatinine, eGFR (a measure of kidney filtering power), and urine tests regularly. · Thyroid problems (hypothyroidism, meaning the thyroid gland slows down and does not make enough hormone) are common—TSH will be checked every 6–12 months. · Tremor (shaky hands) is very common, especially at higher levels. · Increased thirst and frequent urination (nephrogenic diabetes insipidus, where the kidneys ignore the signal to save water) happen often. · Nausea, diarrhea, and stomach upset are common, especially when starting. · Weight gain can occur. · Toxicity signs (confusion, slurred speech, severe tremor, vomiting, seizures) require emergency care—stop the drug and call 911. · Avoid NSAIDs (ibuprofen, naproxen) and diuretics (water pills like hydrochlorothiazide) because they raise lithium levels and can push you into toxicity. · Stay well-hydrated and keep salt intake steady—dehydration or low salt raises lithium levels. · Do NOT use lithium in pregnancy (first trimester risk of Ebstein anomaly, a heart defect) unless no other option exists.

Valproate (divalproex sodium) · Anticonvulsant and mood stabilizer

Valproate increases GABA (gamma-aminobutyric acid, the brain's main calming chemical) by blocking the enzyme GABA transaminase that breaks GABA down, so more GABA stays around to quiet overactive brain circuits. It also blocks voltage-gated sodium channels (tiny gates on brain cells that let electrical signals fire rapidly), which slows down runaway electrical activity. Together, these actions calm the overexcited brain circuits that drive mania.

1. Valproate enters the bloodstream after you swallow it, then crosses into the brain.
2. It blocks the enzyme GABA transaminase, which normally breaks down GABA, so GABA levels rise.
3. More GABA means more inhibitory (calming) signals between brain cells, which slows down overactive circuits.
4. It also blocks voltage-gated sodium channels on brain cells, which stops rapid, repetitive firing (like a brake on runaway electrical activity).
5. Over days to weeks, mania symptoms ease: racing thoughts slow, mood stabilizes, impulsivity drops, and irritability fades.

SAFETY WATCH

Liver damage (hepatotoxicity, meaning the liver becomes inflamed and cannot do its job) is rare but serious, especially in children under 2 and people with genetic metabolic disorders—liver enzymes (AST, ALT) are checked before starting and regularly during treatment. · Pancreatitis (inflammation of the pancreas, causing severe belly pain, nausea, vomiting) is rare but life-threatening—stop the drug and get emergency care if this happens. · Weight gain and increased appetite are very common. · Tremor (shaky hands) is common. · Hair loss (usually temporary and hair grows back) can occur. · Nausea and stomach upset are common, especially when starting—taking it with food or using the extended-release form helps. · Blood disorders: low platelets (thrombocytopenia, which increases bleeding risk) and low white blood cells can occur—complete blood count (CBC) is monitored. · Birth defects: valproate causes serious birth defects (neural tube defects like spina bifida, heart defects, developmental delays, lower IQ) and should NOT be used in pregnancy or in women of childbearing age unless no other option exists and effective birth control is used. · Polycystic ovary syndrome (PCOS) can develop in women, causing irregular periods, weight gain, and excess hair growth. · Hyperammonemia (too much ammonia in the blood, causing confusion and lethargy) can occur—your doctor may check ammonia levels if you become confused.

Carbamazepine · Anticonvulsant and mood stabilizer

Carbamazepine blocks voltage-gated sodium channels (tiny gates on brain cells that let electrical signals fire rapidly). By blocking these channels, it stops brain cells from firing too fast and too often, which calms the overactive circuits that drive mania. It also reduces the release of glutamate (the brain's main excitatory chemical, which speeds up activity) and modulates other pathways that control mood and impulse.

1. Carbamazepine enters the bloodstream after you swallow it, then crosses into the brain.
2. It attaches to voltage-gated sodium channels on brain cells and blocks them, so cells cannot fire rapid, repetitive electrical signals.
3. This reduces overactive signaling in the emotional circuits, calming racing thoughts, irritability, and impulsive behavior.
4. It also reduces the release of glutamate (the brain's main 'speed up' chemical), which further quiets overexcited circuits.
5. Over one to two weeks, mania symptoms ease: mood stabilizes, impulsivity drops, and irritability fades.

SAFETY WATCH

Blood disorders: serious risk of aplastic anemia (the bone marrow stops making enough blood cells) and agranulocytosis (dangerously low white blood cells, which fight infection)—complete blood count (CBC) is checked before starting and regularly during treatment. Stop the drug and call your doctor if you have fever, sore throat, easy bruising, or unusual bleeding. · Stevens-Johnson syndrome and toxic epidermal necrolysis (life-threatening skin reactions causing painful blisters and skin peeling)—stop the drug immediately and get emergency care if a rash appears. People of Asian descent should be tested for the HLA-B*1502 gene before starting, because this gene greatly raises the risk. · Liver damage (hepatotoxicity) can occur—liver enzymes (AST, ALT) are monitored regularly. · Low sodium (Hyponatremia) (low sodium in the blood, causing confusion, weakness, seizures) is common, especially in older adults—sodium levels are checked regularly. · Drug interactions: carbamazepine speeds up the breakdown of many other drugs (including birth control pills, making them less effective), so doses of other medicines may need adjustment. It also lowers its own level over time (auto-induction), so the dose may need to be increased. · Dizziness, drowsiness, and unsteadiness are common, especially when starting. · Nausea and stomach upset are common. · Birth defects (neural tube defects, heart defects, developmental delays) can occur—use effective birth control and discuss risks with your doctor if you could become pregnant.

Lorazepam (a benzodiazepine, used short-term) · Benzodiazepine (sedative-hypnotic)

Lorazepam boosts the effect of GABA (gamma-aminobutyric acid, the brain's main calming chemical) by making GABA-A receptors (tiny gates on brain cells) more sensitive to GABA. When GABA opens these gates, negatively charged chloride ions rush into the cell, making it harder for the cell to fire. This calms overactive circuits, reducing anxiety, agitation, and insomnia. It works fast—within 30 minutes to an hour.

1. Lorazepam enters the bloodstream quickly after you swallow it or it is injected, then crosses into the brain.
2. It attaches to a special site on the GABA-A receptor (a chloride channel on the brain cell surface) and makes the receptor more responsive to GABA.
3. When GABA binds, the channel opens wider and stays open longer, letting more chloride ions flow into the cell.
4. This makes the cell less excitable (harder to fire an electrical signal), which calms anxiety, agitation, and racing thoughts.
5. Within 30–60 minutes, you feel calmer, less agitated, and sleepy—this is a bridge until the mood stabilizer or antipsychotic takes full effect.

SAFETY WATCH

Sedation (feeling very drowsy) is extremely common—do NOT drive or operate machinery. · Risk of dependence (physical need for the drug) and tolerance (needing more to feel the same effect) rise quickly, so use only for short periods (usually less than 2–4 weeks). · Withdrawal symptoms (anxiety, tremor, seizures, confusion, sweating, fast heart rate) can be severe and dangerous if stopped suddenly after regular use—taper off slowly under doctor supervision. · Respiratory depression (breathing slows or stops) is a risk, especially if combined with alcohol, opioids, or other sedatives—never mix these. · Memory problems (anterograde amnesia, meaning you cannot form new memories while the drug is active) can occur. · Falls and confusion are more common in older adults. · Paradoxical reactions (becoming more agitated, aggressive, or disinhibited instead of calm) can happen, especially in children and older adults.

Red flags

- Psychotic symptoms: delusions (fixed false beliefs) or hallucinations (seeing or hearing things that are not there), especially command hallucinations (voices ordering self-harm or violence)
- Suicidal or homicidal thoughts, severe agitation that cannot be calmed, or violent behavior putting the person or others in danger
- Severe insomnia lasting more than 3–5 days straight with escalating energy, impulsivity, and loss of judgment (major crash risk)
- Catatonia (rigid immobility or bizarre posturing), stupor (extreme unresponsiveness), or inability to care for basic needs like eating, drinking, or hygiene
- Signs of lithium toxicity if taking lithium: confusion, coarse tremor (big shaking), loss of coordination (ataxia) (unsteady walking), slurred speech, nausea, vomiting, or seizures

Nursing priorities

1. Assess immediate safety: remove harmful objects, assign one-to-one observation if suicidal or psychotic, and place the patient in a quiet low-stimulation room near the nurses' station — Mania impairs judgment and impulse control, so the brain cannot evaluate danger normally — constant observation prevents self-harm, aggression, or elopement (running away) before medication takes effect

2. Monitor for severe agitation or violence and prepare for rapid chemical or physical restraint if the patient cannot be redirected and poses imminent danger — Severe agitation activates the sympathetic nervous system (fight-or-flight response), raising heart rate and blood pressure dangerously high and increasing injury risk to the patient and staff — early intervention with medication or safe restraint prevents escalation
3. Administer the first dose of antipsychotic medication and benzodiazepine as ordered, monitor vital signs every 15 to 30 minutes after injection, and watch for over-sedation or breathing problems — Antipsychotics block dopamine receptors in the brain to reduce psychosis and agitation, while benzodiazepines enhance GABA (a calming brain chemical) to provide rapid sedation — both can lower blood pressure and slow breathing, especially when combined
4. Ensure the patient eats regular meals and drinks at least 2 liters of fluid daily, offering high-calorie snacks and drinks every 2 hours if the patient is too active to sit for meals — Hyperactivity in mania burns calories faster than normal and the person often forgets to eat or drink due to distraction and racing thoughts — dehydration and low blood sugar worsen confusion and can cause dangerous electrolyte imbalances
5. Monitor sleep duration every shift and report if the patient sleeps less than 4 hours in 24 hours, because ongoing insomnia signals the mania is not controlled — Sleep deprivation worsens mania by disrupting circadian rhythms (the brain's day-night cycle) and stress hormone regulation — restoration of normal sleep is a key marker that treatment is working
6. Check vital signs and watch for fever, muscle rigidity, confusion, or tremor after starting antipsychotic medication, as these are signs of neuroleptic malignant syndrome (a rare life-threatening reaction) — Neuroleptic malignant syndrome happens when dopamine blockade causes the hypothalamus (the brain's temperature control center) to malfunction, leading to dangerously high fever, muscle breakdown, and kidney failure — it requires immediate medical intervention
7. Set firm, calm limits on disruptive behavior using short clear sentences, redirect the patient to safe activities, and avoid arguing about grandiose or delusional beliefs — The manic brain has reduced activity in the prefrontal cortex (the area for self-control and reasoning), so the person cannot process complex explanations or negotiate — simple consistent boundaries reduce frustration and prevent escalation
8. Teach the family that mania is a brain-based medical illness, not willful bad behavior, and give them crisis contact numbers and a follow-up appointment before discharge — Family education reduces shame and improves medication adherence after discharge — mania changes brain chemistry (especially dopamine and norepinephrine systems), and understanding this helps families support treatment instead of blaming the patient

Sources

- American Psychiatric Association DSM-5-TR (2022)
- CANMAT and ISBD 2018 guidelines for the management of patients with bipolar disorder
- APA Practice Guideline for the Treatment of Patients with Bipolar Disorder (2021 update)
- Yatham LN et al., Bipolar Disord 2018 (CANMAT/ISBD)

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