ziprasidone  (zi-pra-si-done)  

**Generic:** None

**Classification:** Antipsychotic, mood stabilizers

**Pharmacologic:** piperazine derivatives

**Pregnancy Category:** C

### Indications

Schizophrenia: IM form is reserved for control of acutely agitated patients. Treatment of acute manic or mixed episodes associated with Bipolar I Disorder (oral only)

### Action

Effect probably mediated by antagonism of dopamine type 2 (D2) and serotonin type 2 (5-HT2). Also antagonizes 2 adrenergic receptors.

### Therapeutic Effects:

Diminished schizophrenic behavior.

### Pharmacokinetics

**Absorption:** 60% absorbed following oral administration; 100% absorbed from IM sites.

**Distribution:** Unknown.

**Protein Binding:** 99%; potential for drug interactions due to drug displacement is minimal.

**Metabolism and Excretion:** 99% metabolized by the liver; 1% excreted unchanged in urine.

**Half-life:** PO—7 hr; IM—2-5 hr.

### TIME/ACTION PROFILE (blood levels)

<table>
<thead>
<tr>
<th>ROUTE</th>
<th>ONSET</th>
<th>PEAK</th>
<th>DURATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>PO</td>
<td>Within hours</td>
<td>1–3 days†</td>
<td>unknown</td>
</tr>
<tr>
<td>IM</td>
<td>Rapid</td>
<td>60 min</td>
<td>unknown</td>
</tr>
</tbody>
</table>

†Steady state achieved following continuous use.

### Contraindications/Precautions

**Contraindicated in:** Hypersensitivity; History of QT prolongation (persistent QTc measurements >500 msec), QT prolongation, recent MI or uncomplicated heart failure.

**Cautions:** Cerebellar ataxia, extrapyramidal symptoms, tardive dyskinesia, depression, suicide attempts, persistent QT prolongation, hyponatremia, electrocardiographic changes. Geriatric patients (may require p doses; p risk of mortality in elderly patients treated for dementia-related psychosis; patients at risk for aspiration pneumonia; history of suicide attempt.

### Adverse Reactions/Side Effects

**CNS:** NEUROLEPTIC MALIGNANT SYNDROME, seizures, dizziness, drowsiness, restless legs, extrapyramidal reactions, syncope, tardive dyskinesia, akathisia, dystonia, hyperreflexia, dysarthria, dyskinesia, fasciculations, tremor, akathisia.

**Resp:** cough, rhinitis.

**CV:** PROLONGED QT INTERVAL, orthostatic hypotension.

**GI:** constipation, diarrhea, nausea, vomiting, dysphagia.

**GU:** amenorrhea, impotence.

**Hemat:** AGRANULOCYTOSIS, leukopenia, neutropenia.

**Endo:** galactorrhea, hyperglycemia, hyperlipidemia, weight gain.

**Derm:** rash, urticaria.

### Interactions

**Drug-Drug:** Concurrent use of quinidine, dofetilide, other class Ia and III antiarrhythmics, propranolol, nadolol, sotalol, propranolol, per- tuzimab, artemisinins, metloquin, delavirdine, tariquidar, dronedarone, and chlorpromazine may result in potentially life-threatening adverse drug reactions (concurrent use contraindicated).

Additive CNS depression may occur with alcohol, antidepressants, antihista- mines, opioid analgesics, or sedative/hypnotics. Blood levels and effectiveness may be altered by carbamazepine. Blood levels and effects may be increased by ketoconazole.

### Route/Dosage

**Schizophrenia**

**PO (Adults):** 20 mg twice daily initially; dose increments may be made at 2-day intervals up to 80 mg twice daily.

Concurrent use of other drugs known to prolong the QT interval including quinidine, delavirdine, propranolol, nadolol, dronedarone, chlorpromazine, pertuzimab, artemisinins, metloquin, delavirdine, tariquidar, and chlorpromazine. 

Use Cautionally in: Concurrent diuretic therapy or dantrolene (may increase the risk of hypotension, hyponatremia, or hyperglycemia), significant hepatic impairment, history of cardiovascular or cerebrovascular disease, Hypersensitivity, concurrent antihypertensive therapy, delirium, or hypothermia (may increase the risk of orthostatic hypotension). 

**GI:** Nausea at 5 risk for extrapyramidal symptoms and weight gain in elderly patients. 

**PO:** Safety not established. 

Geriatric patients (may require p doses; p risk of mortality in elderly patients treated for dementia-related psychosis; patients at risk for aspiration pneumonia; history of suicide attempt.

### Adverse Reactions/Glide Effects

**CNS:** NEUROLEPTIC MALIGNANT SYNDROME, seizures, dizziness, drowsiness, restless legs, extrapyramidal reactions, syncope, tardive dyskinesia, akathisia, dystonia, hyperreflexia, dysarthria, dyskinesia, fasciculations, tremor, akathisia.

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**Derm:** rash, urticaria.

### Interactions

**Drug-Drug:** Concurrent use of quinidine, dofetilide, other class Ia and III antiarrhythmics, propranolol, nadolol, sotalol, propranolol, pertuzimab, artemisinins, metloquin, delavirdine, tariquidar, dronedarone, and chlorpromazine may result in potentially life-threatening adverse drug reactions (concurrent use contraindicated).

Additive CNS depression may occur with alcohol, antidepressants, antihista- mines, opioid analgesics, or sedative/hypnotics. Blood levels and effectiveness may be altered by carbamazepine. Blood levels and effects may be increased by ketoconazole.

### Route/Dosage

**Schizophrenia**

**PO (Adults):** 20 mg twice daily initially; dose increments may be made at 2-day intervals up to 80 mg twice daily.
IM (Adults): 10–20 mg as needed up to 40 mg/day; may be given as 10 mg every 2 hr or 20 mg every 4 hr.

Acute Manic or Mixed Episodes Associated with Bipolar I Disorder

PO (Adults): 40 mg twice on first day, then 60 or 80 mg twice daily on second day; then 40–80 mg twice daily.

Maintenance Treatment of Bipolar I Disorder (as adjunct to lithium or valproate)

PO (Adults): Continue same dose on which patient was initially stabilized (range: 40–80 mg twice daily).

NURSING IMPLICATIONS

Assessment
- Monitor patient’s mental status (orientation, mood, behavior) prior to and periodically during therapy.
- Assess weight and BMI initially and periodically during therapy.
- Monitor BP (sitting, standing, lying) and pulse rate prior to and frequently during initial dose titration.
- Patients found to have persistent QTc measurements of \( \geq 500 \) msec should have ziprasidone discontinued.
- Patients who experience dizziness, palpitations, or syncope may require further evaluation (i.e., Holter monitoring).
- Assess for rash during therapy. May be treated with antihistamines or corticosteroids. Usually resolves upon discontinuation of ziprasidone. Medication should be discontinued if no alternative etiology for rash is found.
- Observe carefully when administering medication to ensure medication is actually taken and not hoarded or cheeked.
- Monitor for onset of akathisia (restlessness or desire to keep moving) and extrapyramidal side effects (parkinsonism—difficulty speaking or swallowing, loss of balance control, pill rolling of hands, mask-like face, shuffling gait, rigidity, tremors and dystonic muscle spasm, twisting motions, uncontrolled chewing and dystonic muscle spasms, twisting motions, twitching, inability to move eyes, weakness of arms or legs) every 2 mo during therapy and 8–12 wk after therapy has been discontinued. Notify health care professional if these symptoms occur, as reduction in dose or discontinuation of medication may be necessary. Trihexyphenidyl or benztropine may be used to control these symptoms.
- Although not yet reported for ziprasidone, monitor for possible tardive dyskinesia (uncontrolled rhythmic movement of mouth, face, and extremities, lip smacking or puckering, pulling of cheeks, uncontrolled chewing, rapid or worm-like movements of tongue). Report these symptoms immediately, as they may be irreversible.
- Monitor frequency and consistency of bowel movements. Increasing bulk and fluids may help to minimize constipation.
- Appropriate lower the serum threshold for seizure precautions for patients with history of seizure disorder.
- Monitor for development of neuroleptic malignant syndrome (fever, respiratory distress, tachycardia, seizures, diaphoresis, hyperpyrexia or hypotension, pallor, tachycardia). Notify health care professional immediately if these symptoms occur.
- Monitor for symptoms related to hyperprolactinemia (mammary abnormalities, galactorrhea, sexual dysfunctions).

- Lab Test Considerations: Monitor serum potassium and magnesium prior to and periodically during therapy. Patients with low potassium or magnesium should have levels treated and check prior to resuming therapy. Obtain fasting blood glucose and cholesterol levels initially and periodically during therapy.
- Monitor CBC frequently during initial months of therapy in patients with pre-existing or history of low WBC. May cause leukopenia, neutropenia, or agranulocytosis. Discontinue therapy if these occur.
- Monitor serum prolactin prior to and periodically during therapy. May cause \( \geq 3 \) serum prolactin levels.

Potential Nursing Diagnoses

Risk for other-directed violence (Indications)

Disturbed thought process (Indications)

Imbalanced nutrition: risk for more than body requirements (Side Effects)

Implementation

- Dose adjustments should be made at intervals of no less than 2 days. Usually patients should be observed for several weeks before dose titration.
- Patients on parenteral therapy should be converted to oral doses as soon as possible.
- PO: Administer capsules whole or with a decrease gastric irritation. Swallow capsules whole; do not open.
- IM: Add 1.2 mL of Sterile Water for Injection to the vial; shake vigorously until all drug is dissolved for a concentration of 20 mg/mL. Discard unused portion. Do not mix with other products or solutions. Do not administer solutions that are discolored or contain particulate matter.

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CONTINUED
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 Ziprasidone

**Patient/Family Teaching**
- Instruct patient to take medication as directed, at the same time each day. Do not discontinue medication without discussing with health care professional, even if feeling well. Patients on long-term therapy may need to discontinue gradually.
- Instruct patient of possibility of extrapyramidal symptoms. Instruct patient to report these symptoms immediately.
- Advise patient to change positions slowly to minimize orthostatic hypotension.
- May cause somnolence and dizziness. Caution patients to avoid driving or other activities requiring alertness and to consult health care professional.
- Advise patient to notify health care professional of all Rx or OTC medications, vitamins, or herbal products being taken, and to consult health care professional before taking other medications. Caution patient to avoid concurrent use of alcohol and other CNS depressants.
- Advise patient to notify health care professional of medication regimen prior to treatment or surgery.
- Instruct patient to notify health care professional promptly if dizziness, loss of consciousness, palpitations, menstrual abnormalities, galactorrhea or sexual dysfunction occur.
- Advise female patients to notify health care professional if pregnancy is planned or suspected, or if breast feeding or planning to breast feed.
- Advise patient to notify health care professional of need for continued medical follow-up for psychotherapy, eye exams, and laboratory tests.
- Instruct patient to keep eye drops in cold, unopened container in refrigerator. Do not reuse after eye drops have been instilled.

**Evaluation/Desired Outcomes**
- Decrease in acute excited, manic behavior.
- Decrease in positive (delusions, hallucinations) and negative symptoms (social withdrawal, flat, blunted affect) of schizophrenia.
- Management of signs and symptoms of Bipolar I Disorder.

**Why was this drug prescribed for your patient?**

- Generic Implication
- Discontinued