QUETIAPINE

THERAPEUTICS

Brands
• Seroquel, Ketipinor, Seroquel XR

Generic?  In some countries

Class
• Atypical antipsychotic

Commonly Prescribed for
(FDA approved in bold)
• Schizophrenia
• Bipolar disorder (depression and acute mania)
• Major depressive disorder (adjunctive)
• Psychosis in patients with Parkinson’s disease (PD) or dementia with Lewy bodies (DLB)
• Obsessive-compulsive disorder
• Autism
• Alcoholism
• Tourette syndrome
• Insomnia
• Anxiety

How the Drug Works
• Blocks D2 receptor similar to other neuroleptics, but also blocks serotonin 2A receptors, which improves motor side effects and perhaps depression and cognitive problems
• May also affect serotonin 1A and other receptors, contributing to efficacy for cognitive and affective symptoms in some patients

How Long Until It Works
• Psychosis – may be effective in days, more commonly takes weeks or months to determine best dose and achieve best clinical effect. Usually 4–6 weeks
• Insomnia – may be effective immediately

If It Works
• Continue to use at lowest required dose. Most patients with schizophrenia see a reduction in psychosis with quetiapine (and other neuroleptics), but some patients, including many with PD and DLB, may improve more than 50%

If It Doesn’t Work
• Increase dose

• In psychosis related to PD or DLB, reduce dose or eliminate offending medications, such as dopamine agonists or amantadine
• If not effective consider changing to clozapine. In PD and DLB, avoid long-term use of conventional antipsychotics
• Insomnia: if no sedation occurs despite adequate dosing, change to another agent

Best Augmenting Combos for Partial Response or Treatment-Resistance
• Patients with affective disorders, such as bipolar disorder, may respond to mood stabilizing anticonvulsants, lithium, or benzodiazepines. In PD and DLB, cholinesterase inhibitors may improve symptoms (particularly in DLB).

Tests
• Prior to starting treatment and periodically during treatment, monitor weight, blood pressure, lipids, and fasting glucose due to risk of metabolic syndrome

ADVERSE EFFECTS (AEs)

How Drug Causes AEs
• Motor AEs – blocking of D2 receptors
• Sedation, weight gain – blocking of histamine 1 receptors
• Hypotension – blocking of alpha-1 adrenergic receptors
• Dry mouth, constipation – blocking of muscarinic receptors

Notable AEs
• Most common: sedation, weight gain, constipation, dry mouth,
• Less common: dizziness, tachycardia, nausea, akathisia, elevation of hepatic transaminases. May increase risk of cataracts

Life-Threatening or Dangerous AEs
• Tardive dyskinesias (lower than other neuroleptics)
• Severe weight gain and metabolic syndrome/diabetes
• Neuroleptic malignant syndrome (rare compared with conventional antipsychotics)
QUETIAPINE (continued)

Weight Gain
• Common

Sedation
• Problematic

What to Do About AEs
• Take at night: for many disorders there is no need for daytime dosing. Medical management for obesity, including weight loss and exercise, may help combat weight gain

Best Augmenting Agents for AEs
• Most AEs cannot be improved with an augmenting agent

DOSING AND USE

Usual Dosage Range
• Bipolar disorder/schizophrenia: 150–800 mg/day
• Psychosis in PD/DLB: 25–200 mg/day

Dosage Forms
• Capsules: 25 mg, 50 mg, 100 mg, 200 mg, 300 mg
• Extended release: 50 mg, 150 mg, 200 mg, 300 mg, 400 mg

How to Dose
• Start at 25 mg twice a day for acute psychosis or mania. If not tolerated, give larger dose in the evening. Increase by 25–50 mg (twice a day) every 1–2 days until effective dose is reached
• For depression or psychosis with PD or DLB, consider dosing all the medication at night. Start PD and DLB patients with psychosis on 12.5 mg at night and increase by 12.5 mg every 1–2 days until symptoms improve. Most patients respond to a lower dose (average 50–75 mg/day)
• Titrate more rapidly when treating acute mania or schizophrenia — up to 800 mg/day in some cases

Dosing Tips
• Patients with bipolar disorder (mania or depression) often need a high dose (over 400 mg/day) to achieve best results. Elderly and children often need lower doses

Overdose
• Sedation, hypotension, bradycardia, and dysarthria have been reported. Death is rare

Long-Term Use
• Safe for long-term use with appropriate monitoring

Habit Forming
• No, although may be used by addicts to manage drug withdrawal

How to Stop
• No need to taper, but psychosis or insomnia often recurs

Pharmacokinetics
• Hepatic metabolism to inactive metabolites via CYP450 3A and 2D6. Half-life 6–7 hours, and steady state reached in 2 days

Drug Interactions
• CYP3A and 2D6 inhibitors (ketoconazole, erythromycin, ciprofloxacin, duloxetine) and valproate may increase levels
• Enzyme inducers, such as phenobarbital, carbamazepine, phenytoin, increase clearance and may lower levels
• Quetiapine may slightly lower levels of valproate and lorazepam

Other Warnings/Precautions
• May increase risk of cataracts, aspiration pneumonia, and priapism

Do Not Use
• Proven hypersensitivity to quetiapine
### Special Populations

<table>
<thead>
<tr>
<th>Renal Impairment</th>
<th>No dose adjustment needed</th>
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</thead>
<tbody>
<tr>
<td>Hepatic Impairment</td>
<td>Use with caution. May need to lower dose</td>
</tr>
<tr>
<td>Cardiac Impairment</td>
<td>May worsen orthostatic hypotension. Use with caution</td>
</tr>
<tr>
<td>Elderly</td>
<td>Start with lower doses. Clearance reduced by about 40%</td>
</tr>
<tr>
<td>Children and Adolescents</td>
<td>Efficacy and safety unknown, but occasionally used for affective disorders. Monitor for weight gain and other AEs</td>
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<tr>
<td>Pregnancy</td>
<td>Category C. Probably safer than anticonvulsants during pregnancy for bipolar disorder. PD and DLB are uncommon in women of childbearing age. Use only if benefit outweighs risks</td>
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<tr>
<td>Breast Feeding</td>
<td>Unknown if found in breast milk. Use while breast feeding is generally not recommended</td>
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### The Art of Neuropharmacology

#### Potential Advantages
- Useful in controlling psychosis associated with PD at relatively low doses without risk of drug-induced parkinsonism or tardive dyskinesias. No risk of blood dyscrasias

#### Potential Disadvantages
- Probably less effective than clozapine. Does not usually improve motor symptoms of PD. Risk of weight gain and metabolic syndrome

#### Primary Target Symptoms
- Psychosis, depression, mania, and insomnia

#### Pearls
- Clozapine, formerly the first-line agent for psychosis with PD, is now often a second-line agent due to risk of agranulocytosis. Use low doses and titrate much more slowly when treating PD or DLB with neuroleptics compared to patients with mania or schizophrenia
- Previous studies suggested usefulness in treating psychosis in patients with Alzheimer’s dementia, but subsequently shown to worsen cognitive function with significant AEs
- Often effective at low doses for insomnia, but not recommended as a first-line option. Atypical antipsychotics increase mortality when used to treat dementia-related psychosis

(continued) QUETIAPINE
QUETIAPINE (continued)

Suggested Reading


