Seroquel (quetiapine fumarate) - Drug Summary

AstraZeneca Pharmaceuticals LP

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Seroquel (quetiapine fumarate)

BOXED WARNING

Elderly patients w/ dementia-related psychosis treated w/ antipsychotic drugs are at an increased risk of death. Not approved for the treatment of patients w/ dementia-related psychosis. Antidepressants increased the risk of suicidal thoughts and behavior in children, adolescents, and young adults in short-term studies. Monitor closely for worsening, and for emergence of suicidal thoughts and behaviors in patients who are started on antidepressant therapy. Not approved for use in pediatric patients <10 yrs of age.

THERAPEUTIC CLASS

Atypical antipsychotic

DEA CLASS

RX

ADULT DOSAGE & INDICATIONS

Schizophrenia

Day 1: 25mg bid
Days 2-3: Increase by 25-50mg divided bid or tid to a range of 300-400mg by Day 4
Titrate: Further adjustments can be made in increments of 25-50mg bid, in intervals of ≥2 days
Recommended Dose: 150-750mg/day
Max: 750mg/day

Maint:
Recommended Dose: 400-800mg/day
Max: 800mg/day

Switching from Depot Antipsychotics:
Initiate quetiapine therapy in place of the next scheduled inj if medically appropriate

Bipolar I Disorder

Acute Treatment of Manic Episodes:
Monotherapy/Adjunct to Lithium or Divalproex:
Day 1: 100mg/day given bid
Day 2: 200mg/day given bid
Day 3: 300mg/day given bid
Day 4: 400mg/day given bid
Titrate: Further adjustments up to 800mg/day by Day 6 should be in increments of ≤200mg/day
Recommended Dose: 400-800mg/day
Max: 800mg/day

Maint Treatment of Bipolar I Disorder as Adjunct to Lithium or Divalproex:
Recommended Dose: 400-800mg/day given bid
Max: 800mg/day

Bipolar Disorder

Acute Treatment of Depressive Episodes:
Monotherapy:
Day 1: 50mg qhs
Day 2: 100mg qhs
Day 3: 200mg qhs

Day 4: 300mg qhs
Recommended Dose: 300mg/day
Max: 300mg/day

PEDIATRIC DOSAGE & INDICATIONS

Schizophrenia

13-17 Years:
Day 1: 25mg bid
Day 2: 100mg/day given bid
Day 3: 200mg/day given bid
Day 4: 300mg/day given bid
Day 5: 400mg/day given bid
Titrate: Further adjustments should be in increments ≤100mg/day
Recommended Dose: 400-800mg/day
Max: 800mg/day

May administer tid based on response and tolerability

Switching from Depot Antipsychotics:
Initiate quetiapine therapy in place of the next scheduled inj if medically appropriate

Bipolar I Disorder

Acute Treatment of Manic Episodes:
10-17 Years:
Monotherapy:
Day 1: 25mg bid
Day 2: 100mg/day given bid
Day 3: 200mg/day given bid
Day 4: 300mg/day given bid
Day 5: 400mg/day given bid
Titrate: Further adjustments should be in increments ≤100mg/day
Recommended Dose: 400-600mg/day
Max: 600mg/day

May administer tid based on response and tolerability

DOSING CONSIDERATIONS

Concomitant Medications
CYP3A4 Inhibitors:
Reduce quetiapine dose to 1/6 of original dose when coadministered
When CYP3A4 inhibitor is discontinued, increase quetiapine dose by 6-fold

CYP3A4 Inducers:
Increase quetiapine dose up to 5-fold of the original dose when used in combination w/ a chronic treatment (eg, >7-14 days) of a potent CYP3A4 inducer
When CYP3A4 inducer is discontinued, reduce quetiapine dose to original level w/in 7-14 days

Hepatic Impairment
Initial: 25mg/day
Titrate: May increase by 25-50mg/day

Elderly
Initial: 50mg/day
Titrate: May increase by 50mg/day

Other Important Considerations
Debilitated Patients/Predisposed to Hypotension:
Consider slower rate of titration and lower target dose

Reinitiation of Treatment in Patients Previously Discontinued:
Discontinued <1 Week: Reinitiate maint dose
Discontinued >1 Week: Follow initial dosing schedule

ADMINISTRATION

Oral route

Take w/ or w/o food.

HOW SUPPLIED

Tab: 25mg, 50mg, 100mg, 200mg, 300mg, 400mg

WARNINGS/PRECAUTIONS

Initiate in pediatric patients only after a thorough diagnostic evaluation is conducted and careful consideration is given to the risks of therapy. Neuroleptic malignant syndrome (NMS) reported; d/c and institute symptomatic treatment. Associated w/ metabolic changes that include hyperglycemia/diabetes mellitus (DM), dyslipidemia, and body weight gain. May cause tardive dyskinesia (TD), especially in the elderly; consider discontinuation if this occurs. May induce orthostatic hypotension; caution w/ known cardiovascular/cerebrovascular disease or conditions that predispose patients to hypotension. May increase BP in children and adolescents. Leukopenia, neutropenia, and agranulocytosis reported; d/c at 1st sign of decline in WBC count w/o causative factors in patients w/ preexisting low WBC count or a history of drug induced leukopenia/neutropenia. D/C therapy and follow WBC count until recovery in patients w/ severe neutropenia (ANC <1000/mm^3). Lens changes reported during long-term treatment. May prolong QT interval; avoid in circumstances that may increase the risk of torsades de pointes and/or sudden death. Seizures reported; caution w/ conditions that lower seizure threshold. Decrease in thyroid hormone levels reported; measure TSH and free T4 at baseline and at follow-up in addition to clinical assessment. May elevate prolactin levels. May impair physical/mental abilities. May disrupt body's ability to reduce core body temperature. May cause esophageal dysmotility and aspiration; caution in patients at

risk for aspiration pneumonia. Acute withdrawal symptoms (eg, N/V, insomnia) may occur after abrupt cessation; d/c gradually.

ADVERSE REACTIONS

Headache, somnolence, dizziness, dry mouth, constipation, dyspepsia, tachycardia, asthenia, agitation, pain, weight gain, ALT increased, abdominal pain, postural hypotension, N/V.

DRUG INTERACTIONS

See Dosing Considerations. Caution w/ other centrally acting drugs and alcohol. Increased exposure w/ CYP3A4 inhibitors (eg, ketoconazole, ritonavir, nefazodone) and decreased exposure w/ CYP3A4 inducers (eg, phenytoin, carbamazepine, rifampin). May enhance the effects of certain antihypertensives. May antagonize the effects of levodopa and dopamine agonists. QT prolongation reported w/ drugs known to cause electrolyte imbalance. Avoid w/ other drugs that are known to prolong QTc interval (eg, quinidine, amiodarone, ziprasidone). Caution w/ anticholinergic medications.

PREGNANCY AND LACTATION

Pregnancy: Category C.
Lactation: Not for use in nursing.

MECHANISM OF ACTION

Dibenzothiazepine derivative; not established. Suspected to be mediated through a combination of dopamine type 2 and serotonin type 2 antagonism.

PHARMACOKINETICS

Absorption: Rapid. T_{max}=1.5 hrs. **Distribution:** V_d=10L/kg; plasma protein binding (83%); found in breast milk. **Metabolism:** Liver (extensive) via sulfoxidation and oxidation (CYP3A4); N-desalkyl quetiapine (active metabolite). **Elimination:** Urine (approx 73%), feces (approx 20%); $T_{1/2}$=6 hrs.

ASSESSMENT

Assess for history of dementia-related psychosis, risk for hypotension, drug hypersensitivity, psychiatric disorders, hepatic impairment, other conditions where treatment is cautioned, pregnancy/nursing status, and possible drug interactions. Obtain baseline FPG in patients w/ DM or at risk for DM. Obtain baseline CBC if at risk for leukopenia/neutropenia. Obtain baseline TSH and free T4. Obtain baseline BP in children and adolescents. Assess for cataracts by performing lens exam (eg, slit-lamp exam).

MONITORING

Monitor for clinical worsening, suicidality, unusual changes in behavior, NMS, TD, hyperglycemia, orthostatic hypotension, hypothyroidism, seizures, aspiration, and other adverse effects. Monitor CBC frequently during 1st few months in patients w/ preexisting low WBC count or history of drug-induced leukopenia/neutropenia. Monitor for fever or other signs/symptoms of infection in patients w/ neutropenia. Monitor weight regularly, and lipids, hepatic function, and FPG periodically. Monitor for cataract formation shortly after start of treatment, and at 6-month intervals during chronic treatment. Monitor BP periodically during treatment in children and adolescents. Periodically reassess for continued need for maintenance treatment.

PATIENT COUNSELING

Inform of the risks and benefits of therapy. Instruct caregivers and patients to contact physician if signs of agitation, anxiety, panic attacks, insomnia, hostility, aggressiveness, impulsivity, akathisia, hypomania, mania, irritability, worsening of depression, changes in behavior, or suicidal ideation develop. Advise about signs/symptoms of NMS, symptoms of hyperglycemia and DM, weight gain, and risk of orthostatic hypotension. Instruct to avoid overheating and dehydration. Caution about performing activities requiring mental alertness. Instruct to notify physician if patient becomes pregnant or intends to become pregnant during therapy, and if patient is taking or plans to take any prescription or OTC drugs.

STORAGE

25°C (77°F); excursions permitted to 15-30°C (59-86°F).

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