Geodon (ziprasidone hydrochloride); (ziprasidone mesylate) - Drug Summary

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Geodon
(ziprasidone hydrochloride, ziprasidone mesylate)

BOXED WARNING

Elderly patients w/ dementia-related psychosis treated w/ antipsychotic drugs are at an increased risk of death; most deaths appeared to be cardiovascular (CV) (eg, heart failure [HF], sudden death) or infectious (eg, pneumonia) in nature. Not approved for treatment of dementia-related psychosis.

THERAPEUTIC CLASS

Atypical antipsychotic

DEA CLASS

RX

ADULT DOSAGE & INDICATIONS

Schizophrenia

Cap:
Initial: 20mg bid
Titrate: May adjust up to 80mg bid at intervals of not <2 days
Max: 80mg bid

Maint Treatment: No additional benefit demonstrated for doses >20mg bid

Acute Agitation in Schizophrenia:
IM:
10mg (may give q2h) to 20mg (may give q4h)
Max: 40mg/day

IM administration for >3 consecutive days has not been studied; if long-term therapy is indicated, replace w/ oral formulation as soon as possible

Bipolar I Disorder

Mixed or Manic Episodes:
Cap:
Acute (Monotherapy):
Initial: 40mg bid
Titrate: May increase to 60mg or 80mg bid on 2nd day of treatment, and subsequently adjust based on tolerance and efficacy w/in the range 40-80mg bid

Maint (Adjunct to Lithium or Valproate):
Continue treatment at the same dose on which the patient was initially stabilized, w/in the range of 40-80mg bid

DOSING CONSIDERATIONS

Elderly
Start at lower end of dosing range

ADMINISTRATION

Oral/IM route

Cap
Take w/ food.

IM
Add 1.2mL of sterile water for inj (SWFI) to vial and shake vigorously until all the drug is dissolved.
Draw up 0.5mL of reconstituted sol to administer a 10mg dose; draw up 1mL of reconstituted sol to administer a 20mg dose.
Do not mix w/ other medicinal products or solvents other than SWFI.

HOW SUPPLIED

Cap: 20mg, 40mg, 60mg, 80mg; **Inj:** 20mg/mL

CONTRAINDICATIONS

Recent acute MI, uncompensated HF, or known history of QT prolongation (including congenital long QT syndrome). Concomitant use w/ dofetilide, sotalol, quinidine, other class IA/III antiarrhythmics, mesoridazine, thioridazine, chlorpromazine, droperidol, pimozide, sparfloxacin, gatifloxacin, moxifloxacin, halofantrine, mefloquine, pentamidine, arsenic trioxide, levomethadyl acetate, dolasetron mesylate, probucol, tacrolimus, or other drugs that prolong QT interval.

WARNINGS/PRECAUTIONS

Avoid in patients w/ history of cardiac arrhythmias. D/C in patients w/ persistent QTc measurements >500 msec. Hypokalemia and/or hypomagnesemia may increase risk of QT prolongation and arrhythmia; replete those electrolytes before treatment. Initiate further evaluation if symptoms of torsades de pointes occur. Neuroleptic malignant syndrome (NMS) reported; d/c therapy and institute symptomatic treatment. Drug reaction w/ eosinophilia and systemic symptoms (DRESS) and other severe cutaneous reactions reported; d/c if suspected. May cause tardive dyskinesia (TD), especially in the elderly; consider discontinuation if this occurs. Associated w/ metabolic changes (eg, hyperglycemia, dyslipidemia, weight gain) that may increase CV/cerebrovascular risk. Rash and/or urticaria reported; d/c upon appearance of rash. May induce orthostatic hypotension and syncope; caution w/ CV disease, cerebrovascular disease, or conditions that predispose to hypotension. Leukopenia, neutropenia, and agranulocytosis reported; d/c in patients w/ severe neutropenia (ANC <1000/mm^3) or at 1st sign of decline in WBCs in patients w/ preexisting low WBC count or history of drug-induced leukopenia/neutropenia. Seizures reported. May cause esophageal dysmotility and aspiration; caution in patients at risk for aspiration pneumonia. May elevate prolactin levels. May impair physical/mental abilities. Somnolence and priapism reported. May disrupt the body's ability to reduce core body temperature. Caution in cardiac patients and in those at risk for suicide. Caution w/ renal impairment when administered IM. Concomitant use of IM and oral preparations in schizophrenic patients is not recommended.

ADVERSE REACTIONS

N/V, rash, diarrhea, somnolence, dizziness, headache, extrapyramidal symptoms, respiratory tract infection, akathisia, abnormal vision, asthenia, constipation, dry mouth, anxiety. **Inj:** Inj-site pain.

DRUG INTERACTIONS

See Contraindications. Caution w/ centrally acting drugs and medications w/ anticholinergic activity. May enhance effects of certain antihypertensives. May antagonize effects of levodopa and dopamine agonists. Decreased exposure w/ carbamazepine. Increased levels w/ CYP3A4 inhibitors (eg, ketoconazole). Periodically monitor serum electrolytes w/ diuretics.

PREGNANCY AND LACTATION

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

MECHANISM OF ACTION

Atypical antipsychotic; mechanism not established. Proposed that efficacy in schizophrenia is mediated through a combination of dopamine type 2 and serotonin type 2 antagonism.

PHARMACOKINETICS

Absorption: (Oral) Well-absorbed. Absolute bioavailability (approx 60%); T_{max}=6-8 hrs. (IM) Absolute bioavailability (100%); T_{max}=60 min. **Distribution:** (Oral) V_d=1.5L/kg; plasma protein binding (>99%). **Metabolism:** (Oral) Liver (extensive) via aldehyde oxidase (primary), CYP3A4 and CYP1A2; benzisothiazole (BITP) sulphoxide, BITP-sulphone, ziprasidone sulphoxide, and S-methyldihydroziprasidone (major metabolites). **Elimination:** (Oral) Urine (20%, <1% unchanged), feces (66%, <4% unchanged); $T_{1/2}$=7 hrs. (IM) $T_{1/2}$=2-5 hrs.

ASSESSMENT

Assess for drug hypersensitivity, history of QT prolongation, recent acute MI, uncompensated HF, dementia-related psychosis, history of seizures/conditions that lower seizure threshold, other conditions where treatment is contraindicated or cautioned, pregnancy/nursing status, and possible drug interactions. Obtain baseline serum electrolytes (K^+, Mg^{2+}) in patients at risk for significant electrolyte disturbances. Obtain baseline FPG in patients w/ diabetes mellitus (DM) or at risk for DM. Obtain baseline CBC if at risk for leukopenia/neutropenia.

MONITORING

Monitor for QT prolongation, torsades de pointes, NMS, DRESS and other severe cutaneous reactions, TD, metabolic changes, rash, orthostatic hypotension, seizures, esophageal dysmotility, aspiration, suicidal ideation, hypokalemia, hypomagnesemia, and other adverse reactions. Monitor CBC frequently during the 1st few months of therapy in patients w/ preexisting low WBCs or history of drug-induced leukopenia/neutropenia. Monitor for fever or other signs/symptoms of infection in patients w/ neutropenia. Monitor for worsening of glucose control in patients w/ DM and monitor FPG in patients at risk for DM. Reassess periodically to determine need for maintenance treatment.

PATIENT COUNSELING

Inform of the risks and benefits of therapy. Advise to inform physician of any history of QT prolongation, recent acute MI, uncompensated HF, risk for electrolyte abnormalities, history of cardiac arrhythmia, or if taking other QT-prolonging drugs. Instruct to report conditions that increase risk for electrolyte disturbances (eg, hypokalemia, taking diuretics, prolonged diarrhea) and if dizziness, palpitations, or syncope occurs. Instruct to report to physician at the earliest onset any signs/symptoms that may be associated w/ DRESS or w/ severe cutaneous reactions (eg, Stevens-Johnson syndrome).

STORAGE

25°C (77°F); excursions permitted to 15-30°C (59-86°F). **Inj:** Protect from light. **Reconstituted Sol:** 15-30°C (59-86°F) for up to 24 hrs when protected from light, or at 2-8°C (36-46°F) for up to 7 days.

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