

The Carlat Psychiatry Report

CLOZAPINE Fact Sheet

Manufacturer: Novartis; also available in generic formulations.

Indications:

- Management of severely ill schizophrenic patients who fail to respond to standard drug treatment.
- Reduction in the risk of suicide in schizophrenia and schizoaffective disorder.
- Off-label use for a variety of disorders, including bipolar and schizoaffective disorder.

Mechanism: Antagonist of several dopamine receptors.

Dosing:

- Supplied in 25 mg and 100 mg breakable tablets.
- Start at 12.5 mg QD or BID, and increase gradually by 25-50 mg/day to target dose of 300-450 mg after 2 weeks. Maximum recommended dose is 900 mg/day divided TID.
- It may take 3 to 6 months for a therapeutic response.

Side effects:

- Most common are sedation, dizziness, hypersalivation (no good treatment; place towel on pillow), weight gain (substantial, 15-30 pound average wt. gain after one year), constipation, tachycardia (can treat with inderal).
- EPS: Uncommon.
- Glucose/Lipids: Associated with new onset diabetes and hyperlipidemia; worse in this regard than all atypicals.
- EKG: No clear changes.
- Prolactin level: Little or no increase.
- Pregnancy category B.
- **BLACK BOX WARNINGS:** *Agranulocytosis:* Most cases occur during the first 3 months of treatment. Incidence is 0.4%, and death rate is 0.012% (1 out of 10,000 patients); *Seizures:* About 5% incidence. Can be managed by reducing dose or adding Depakote; *Myocarditis:* Rare but often fatal; *Cardiovascular collapse:* 1/3000 patients; *Mortality in elderly patients:* 1.7 times the risk of placebo (class warning for all atypicals).

Drug-drug interactions:

- Does not affect hepatic enzyme systems, thus does not affect metabolism of other drugs.
- Luvox, Tagamet, and erythromycin inhibit the metabolism of clozapine and therefore can increase blood levels.
- Tegretol and nicotine induce clozapine metabolism and can decrease blood levels.
- Half-life 12 hours.

Laboratory Monitoring: U.S. monitoring requirements: Weekly WBC for first 6 months, then every other week. After one year of normal WBCs, can reduce frequency of monitoring to monthly.