CLOZAPINE:

Class: Atypical Antipsychotic

Indications: Treatment-refractory schizophrenia

Available dosage form in the hospital: TAB **(**25MG, 100 MG**)**

Trade Names:

Dosage: **Note:** When converting a patient from other antipsychotics to clozapine therapy, the dosage of the other antipsychotics should be reduced or discontinued (based on clinical circumstances) by gradual tapering downwards before initiating clozapine. Combination use with other antipsychotics is not generally recommended.

-**Schizophrenia:** Oral: Initial: 12.5 mg once or twice daily; increased, as tolerated, in increments of 25-50 mg daily to a target dose of 300-450 mg daily by the end of 2 weeks; may further titrate in increments not exceeding 100 mg and no more frequently than once or twice weekly. May require doses as high as 600-900 mg daily (maximum dose: 900 mg daily). **Note:** In some efficacy studies, total daily dosage was administered in 3 divided doses.

-**Suicidal behavior in schizophrenia or schizoaffective disorder:** Oral: Initial: 12.5 mg once or twice daily; increased, as tolerated, in increments of 25-50 mg daily to a target dose of 300-450 mg daily by the end of 2 weeks; mean dose is ~300 mg daily (range: 12.5-900 mg); treatment duration 2 years then reassess need (based on suicide risk). **Note:** If no longer a suicide risk, may resume prior antipsychotic therapy after gradually tapering off clozapine over 1-2 weeks.

-**Bipolar disorder (unlabeled use):** Oral: Initial: 25 mg daily; increased, as tolerated in increments of 25 mg daily to a maximum dose of 550 mg daily. Average daily dose ~300 mg daily (Green, 2000).

-**Schizoaffective disorder (unlabeled use):**Oral: Initial: 25 mg daily; increased, as tolerated to a maximum dose of 600 mg daily. Average daily dose: ~200 mg daily (Ciapparelli, 2003).

Reinitiation of therapy: If dosing is interrupted for ≥48 hours, therapy must be reinitiated at 12.5-25 mg daily; may be increased more rapidly than with initial titration, unless cardiopulmonary arrest occurred during initial titration, then retitrate with extreme caution.

Termination of therapy: In the event of planned termination of clozapine, gradual reduction in dose over a 1- to 2-week period is recommended. If conditions warrant abrupt discontinuation (eg, leukopenia), monitor patient for psychosis and cholinergic rebound (eg, headache, nausea, vomiting, diarrhea, profuse diaphoresis).

Geriatric

Note: When converting a patient from other antipsychotics to clozapine therapy, the dosage of the other antipsychotics should be reduced or discontinued (based on clinical circumstances) by gradual tapering downwards before initiating clozapine. Combination use with other antipsychotics is not generally recommended

-**Schizophrenia:** Oral: Experience in the elderly is limited; may initiate with 12.5 once daily for 3 days, then increase to 25 mg once daily for 3 days as tolerated; may further increase, as tolerated, in increments of 12.5-25 mg daily every 3 days to desired response; maximum total daily dosage: 300 mg (Howanitz, 1999). Mean recommended dosage range: 25-150 mg (in divided doses) (De Fazio, 2003).

-**Psychosis/agitation related to Alzheimer dementia (unlabeled use):** Oral: Initial: 12.5 mg once daily; if necessary, gradually increase as tolerated not to exceed 75-100 mg daily (Rabins, 2007)

Renal Impairment:

No dosage adjustment provided in manufacturer's labeling (has not been studied); use with caution.

Hepatic Impairment:

No dosage adjustment provided in manufacturer's labeling; use with caution.

Common side effect:

Cardiovascular: Tachycardia (25%)

Central nervous system: Drowsiness (39% to 46%), dizziness (19% to 27%), insomnia (2% to 20%)

Gastrointestinal: Sialorrhea (31% to 48%), weight gain (4% to 31%), constipation (14% to 25%), nausea/vomiting (3% to 17%), abdominal discomfort/heartburn (4% to 14%)

Pregnancy Risk Factor B