**Clozapine**

**Clozapine**  Brand name is Clozaril.

- “Atypical” *Antipsychotic medication.
- Used primarily in the treatment of Schizophrenia and Schizoaffective Disorder when other medications have been tried and failed or have caused serious side effects.

The goal of Clozapine therapy is to

- **eliminate** the symptoms of Schizophrenia/Schizoaffective Disorder such as hallucinations and delusions in treatment resistant patients
- **reduction in risk of recurrent suicidal behavior**

*“Atypical” have less extra-pyramidal side effects (tremors, rigidity, dystonia)

**The major side effects of Clozapine**

**Common Side Effects**
Constipation, bedwetting, night-time drooling, muscle stiffness, sedation, drowsiness, dizziness, dry mouth, tremor, orthostatic hypotension, hyperglycemia, weight gain.

**Potential Life Threatening Side Effects**
Agranulocytosis, **Severe neutropenia** [ANC less than 500/mcl], cardiac toxicity, gastrointestinal hypo-motility to bowel obstruction, CNS depression, seizure disorder, bone marrow suppression, myocarditis.

**More Side Effects**
Trouble seeing, increased salivation, restlessness, headache.

**Patient Education to Report the following:** seizures, fainting, uncontrollable shaking, tremors, incontinence, confusion, vision changes, severe muscle stiffness, sweating, unusual/increased bleeding or bruising, loss of appetite, upset stomach, yellowing of eyes or skin, flu-like symptoms, lack of energy, upper right abdominal pain, behavior changes.

**Seek Immediate Help:** dizziness, fainting, slow breathing, heartbeat changes, unconsciousness.

**Why regular blood testing is required?**

**Known Risk of Neutropenia & Myocarditis**
Before starting Treatment need baseline tests:

- **Initial Labs/Testing:**  
  - CBC with diff  
  - EKG  
  - Myocarditis panel [Troponin-I, hs-CRP, BNP]

  - ANC **weekly** first 6 months if acceptable then  
  - ANC **every 2 weeks** for next 6 mos.

  - If Acceptable then every 4 weeks  
  - Additional labs may be recommended

** ***Lab contacts provider and pharmacy if ANC below 1500 GP or 1000 BEN

**What special documentation when order Clozapine?**

- DSM 5 Diagnosis Schizophrenia, Schizoaffective Disorder Refractory Bipolar Disorder or Borderline Personality Disorder
- Treatment Resistance
- Opportunity to Improve Patient’s Quality of Life
- Suicidal/Self Injurious thoughts or behavior
- Violent Behavior
Extrapyramidal Side Effects

- Register with Clozapine REMS Program
- Pharmacy designee to enter ANC results
- Patient Given “What you need to know about Clozapine: A guide for Patients and Caregivers”
- Informed of risk of severe neutropenia associated with Clozapine
- Signed “Clozapine Informed Consent Form”
- Patient willing & able to take oral meds and allow required labs
- **Facility Clozapine Committee** [MH director, attending psychiatrist, medical covering MH, pharmacists, UNC psychiatrists MH Nurse Supervisor/designee]
- **Documentation of labs before start treatment:** CBC with diff Myocarditis panel EKG

FYI:

- Studies demonstrate that clozapine is more effective against treatment resistant schizophrenia than any other antipsychotic.
- Clozapine metabolized in the liver. [s/s hepatotoxicity fatigue, malaise, anorexia, nausea, jaundice, bilirubinemia, hepatic encephalopathy]
- Peak concentration after oral dosing is 2.5 hours. Half-life 14 hours.
- Food does not appear to affect the bioavailability.
- Cigarette smoke inhibits metabolism, hence smokers require up to double the dose of clozapine compared to non-smokers to achieve equivalent plasma levels.
- TD occurs in about 5% of people [below that of typical antipsychotic meds.].
- **Not approved for use in patients with dementia related psychosis.** [Increase risk of death in elderly patients with dementia –related psychosis].

**Several medication interactions:** [This is why a pharmacist is on the treatment team]
- Antibiotics [erythromycin, cipro], antihistamines, cimetidine [Tagamet], bupropion, antihypertensive, oral contraceptives, antiseizure, sedatives, tranquilizers, other MH meds.
- Use of benzodiazepines and clozapine can result in respiratory arrest, cardiac arrest and sudden death.
- Ciprofloxacin elevates clozapine, hence reduction of clozapine dose by 1/3 of original dose while on cipro. Return to original dose when antibiotic course completed.
- Anticholinergic effect leads to clozapine-induced gastrointestinal hypomotility which has a higher cholinergic blockage rate [than other meds], bowel perforation, & rare deaths.

**Nursing** Notify provider:

- Interruption in treatment greater than 48 hrs.
- ANC less than 1500 for GP patients or less than 1000 for BEN pts. [need for further testing]
- If CBC not drawn on designated day, Nurse Supervisor on unit request CBC within 24 hrs.
- signs of infection or myocarditis: **fatigue, dyspnea, chest pain, peripheral edema, persistent palpitations, fever, flu-like symptoms**

If scheduled Labs are late 2 days, pass scheduled time then attending contacted and Clozapine will be discontinued unless CBC immediately obtained.
IMPORTANT TERMS associated with the use of Clozapine:

**Agranulocytosis** - is when too few or no white blood cells (or WBCs) are not made, of them are, reducing the body's ability to resist and fight infection.

**ANC** Absolute Neutrophil Count - WBC [White Blood Cells] % neutrophils

**Antipsychotic Medication** – is psychiatric medication primarily used to manage psychosis (e.g. delusions or hallucinations), particularly in Schizophrenia and Bipolar Disorder. Also called neuroleptics or major tranquilizers.

**BEN** Benign ethnic neutropenia - ethnic group with an average ANC lower than standard. [Normal for the ethnic individuals from African descent, Middle East, other non-Caucians].

**Cardiomyopathy** - diseases of the heart muscle with many causes [genetic or acquired], signs and symptoms, and treatments.

**CBC** Complete Blood Count with differential – blood test what provides the absolute neutrophil count and panic values that conform to the clozapine guidelines.

**GP** General Population [in clozapine monitoring] are all patients without BEN

**Myocarditis** - is inflammation of the heart muscle. A severe case can weaken the heart, which can lead to heart failure, abnormal heartbeat, and sudden death.

**REMS Risk Evaluation and Mitigation Strategy** – strategy to manage known or potential risks associated with a drug or group of drugs. REMS is FDA required for clozapine to ensure the potential benefits outweigh the risk of neutropenia [abnormally low level of neutrophils].

**Schizoaffective disorder** - is a combination of symptoms of schizophrenia and mood disorder, such as depression or bipolar disorder.

**Schizophrenia** - is a severe, chronic, brain disorder that distorts the way a person thinks, acts, expresses emotions, perceives reality and relates to others.

**Related MH TERMS associated with the use of Clozapine:**

**AIMS** – The Abnormal Involuntary Movement Scale (AIMS) records the occurrence of TARDIVE DYSKINESIA (TD) in a patient receiving antipsychotic medications. The AIMS assessment is used to detect TD, and to follow the severity and progression of a patient’s TD over time. AIMS assessments in DPS are done by trained professional staff [psychiatrist, psychologist and trained RNs]

**Akathisia** – is a feeling of inner restlessness with a constant urge to be moving. An individual may be seen pacing the floor. It is peculiar in that while one cannot keep still, the actual movements are voluntary as opposed to other movement disorders, such as tardive dyskinesia which is involuntary. Anti-psychotic medications often induce akathisia.

**Neuroleptic Malignant Syndrome (NMS)** – is a rare but life-threatening neurological disorder most often caused by an adverse reaction to neuroleptic or antipsychotic drugs.

**Tardive Dyskinesia** – TD is a complication of long-term use of antipsychotic medications that is characterized by abnormal involuntary, purposeless, and often repetitive movements of the tongue and muscles of the face, jaw, arms, legs, and trunk. The movements of these body parts often appear rhythmic, writhing, or dance-like. The movement of the legs, arms, and trunk are often rapid.