

CLOZAPINE: Gold Standard Medication for Treatment Resistant Psychosis

Clozapine is currently the most effective antipsychotic medication for treatment-resistant psychosis. Although 20-30% of individuals with schizophrenia are treatment-resistant, in Minnesota only 4.6% use clozapine. Nationwide, the rates range from less than 3% up to 15.6% while in other countries the rates are even higher with Germany at 20%, China at 25% and Australia at 35% ([Treatment Advocacy Center](#)).

Clozapine is Used

- When two antipsychotics have been tried unsuccessfully
- For treatment-resistant psychosis (schizophrenia, schizoaffective disorder and bipolar with psychotic features)
- Suicidal thoughts or self-injurious/aggressive behavior
- For psychosis with movement disorders

Advantages of Clozapine

- Superior efficacy for treatment-resistant symptoms such as hallucinations & delusions
- Reduces suicidality
- Lowers risk of movement disorders
- Reduces aggressive behavior and hostility
- Antidepressant and mood-stabilizing effects
- Lowest all-cause mortality compared to other antipsychotics
- Higher adherence rates and decreased relapse
- Consistently rated highly by patients
- Lower rates of hospitalization and shorter hospital stays
- Improved sleep, social functioning and quality of life
- Improved cognition compared to other antipsychotics
- May decrease substance use, including tobacco

Management of Salient Clozapine Side Effects (*clozapine benefits far outweigh risks for most*)

Common side effects:

- *Constipation prevention*
- *Hypersalivation management*
- *Weight gain/metabolic syndrome treatment*

Rare side effects:

- *Myocarditis*, inflammation of the heart muscle, can occur when hospitals and inexperienced providers titrate clozapine too quickly
- *Neutropenia* is a blood condition that makes people vulnerable to severe infection due to a shortage of white blood cells. Most cases are benign, transient and unrelated to clozapine and most interruptions in treatment due to neutropenia have been unwarranted

Clozapine Risk Evaluation and Mitigation Strategy Program (REMS)

The FDA established Clozapine REMS to manage the risk of developing severe neutropenia. Patients must undergo frequent blood testing monitored by FDA-registered providers and pharmacies which limits access and causes unnecessary and often debilitating delays in obtaining medication. The FDA requires more extensive blood testing for patients using clozapine than for those who use drugs with similar risks. Evidence suggests that the risk of developing severe neutropenia due to clozapine decreases substantially after 18 weeks. At an FDA hearing held on November 19, 2024, an FDA advisory panel voted 14-1 to end REMS clozapine monitoring based on compelling written and oral testimony by patients, families, providers, researchers, associations and others.

Factors Driving Clozapine Underutilization

- Lack of awareness of clozapine and its benefits
- Difficulty finding providers to prescribe clozapine and effectively manage its side effects
- Administrative burden of REMS Program
- Discomfort by providers about clozapine's side effects (although manageable)
- Inconvenience & patient fear/dislike of REMS-required lab draws; home devices now available
- Lack of financial incentives within the healthcare system for the extra time required (REMS)

Minnesota Clozapine Advocacy Initiative

Minnesota partners working to increase the use of lifesaving clozapine. Action steps include:

- Identify and address barriers to clozapine use in Minnesota
- Identify current clozapine providers in our state
- Increase education about and awareness of the benefits of clozapine
- Support family and consumer-led support systems
- Advocate for changes in policy and reimbursement
- Work towards establishing specialized clozapine clinics

You Can Make a Difference

- Join our efforts to expand the use of this gold-standard medication
- Encourage your provider to learn about and begin prescribing clozapine

Helpful Resources

- [The Clozapine Handbook](#), Jonathan M Meyers and Stephen M Stahl
- [Team Daniel Running For Recovery](#)
- [Into the Light Meaningful Recovery from Psychosis Film](#)
- [CURESZ Foundation](#)
- StatPearls, Clozapine, Nov 10, 2023. <https://www.ncbi.nlm.nih.gov/books/NBK535399/>
- The Angry Moms - <https://www.theangrymoms.com/>
- [Schizophrenia and Psychosis Alliance Letter to FDA re: Clozapine REMS](#) (PDF)
- [NAMI Ramsey County Webinar Recording: Clozapine Panel and Listening Session, 4/19/23](#)
- [Treatment Advocacy Center: Clozapine for Treating Schizophrenia: State Comparison](#)
- [Research Weekly: The Clozapine REMS, Aug 2, 2023](#)
- Podcast - Schizophrenia: Three Moms in the Trenches [Episode 18 Rethinking Clozapine](#)
- Podcast - Schizophrenia: Three Moms in the Trenches [Episode 107 Meaningful Recovery in SMI](#)