

Government of Nunavut

Department of Health

OPERATIONAL PROCEDURE

Clozapine Monitoring

Procedure Reference #:**Section:** Pharmacy**Responsibility:** Akausisarvik Mental Health Nurse, Community Health Nurse, Registered Psychiatric Nurse, Attending Physician/Psychiatrist, GenCAN Nurse Co-ordinator**Initial Issue Date:** October 20, 2015**Last Reviewed:** NEW**Revised Date:** NEW**Approved by:** Medical Advisory Committee

PURPOSE

To provide a guideline for the use of Clozapine in Nunavut patients who have been diagnosed with treatment-resistant schizophrenia.

SELECTION CRITERIA

Inclusion:

1. Patients who exhibit an inadequate response to an appropriate course of therapy with another antipsychotic. Can be particularly effective for persistent aggressive behaviour, and suicidal behaviour.
2. Patients who cannot take an effective dose of another antipsychotic due to intolerable adverse effects.
3. Patients with movement disorders secondary to antipsychotic use, such as tardive dyskinesia.
4. Physicians must complete a patient registration form and FAX it to the relevant clozapine registry (see below).

Exclusion:

1. Agranulocytosis (severe low white blood cell count, especially low neutrophil count) or severe granulocytopenia.
 - Patients must meet the following criteria to begin treatment:
 - White Blood Cell (WBC) $> 3.5 \times 10^9/L$, and
 - Absolute Neutrophil Count (ANC) $> 2.0 \times 10^9/L$ (CBC completed within the 28 days prior to initiating treatment)
2. Caution is advised in patients with a history of seizures, underlying cardiovascular disease or arrhythmias.
3. Clozapine is only to be initiated or titrated by a psychiatrist or in consultation with a psychiatrist.
4. Physicians must provide a new registry-specific patient registration form to the dispensing pharmacist prior to switching patients from one brand of clozapine to another.

BACKGROUND

Clozapine is a medication that is commonly used for treatment-resistant schizophrenia. Clozapine may cause a rare but serious complication called agranulocytosis (low white blood cell count). Therefore, clozapine patients must have regular CBC monitoring to ensure that they are not at risk for overwhelming infection.

RESPONSIBILITIES

Manager, Akausisarvik:

- Ensure nurse is assigned to monitor clozapine blood work.
- Ensure replacement nurse coverage for vacations.
- Ensure assigned nurse is trained in using GenCAN database and liaising with GenCAN nurse co-ordinator.

Akausisarvik Mental Health Nurse:

- Register for and regularly monitor online GenCAN patient database.
- Ensure community psychiatric nurses and patients are aware of appropriate blood work schedule.
- Inform community psychiatric nurse when a patient is past due for their regular blood work.
- Co-ordinate with GenCAN Clinical Nurse co-ordinator regarding outstanding blood work and blood test irregularities.
- Liaise with attending psychiatrist regarding management of patients with severe blood work abnormalities and patients that are non-compliant with clozapine medication regimen.
- Ensure QGH laboratory has up-to-date list of Nunavut clozapine patients and standing orders for clozapine bloodwork.

Community Psychiatric Nurse:

- Secure this operating procedure on the inside cover of patient chart for any patient receiving this medication.
- Coordinate blood work to be drawn at the health centre and ensure patient attends blood work appointments on schedule.
- Co-ordinate with Akausisarvik nurse and attending psychiatrist regarding management of severe lab abnormalities and patients who are non-compliant with clozapine regimen.
- Follow up with patient at intervals specified by the prescribing physician and more often as clinically indicated.
- At each patient encounter, the CPN will assess for potential side effects and consult the physician as clinically indicated.
- To consult the Akausisarvik MHN or prescribing physician if unsure how to proceed with medication or blood work regime.
- To document a clear care plan in the patient's chart.

Community Health Nurse:

- Perform psychiatric nurse duties when no psychiatric nurse is available in community.
- To draw blood work, as per prescribing physician orders.
- At each patient encounter, the CHN will assess for potential side effects and consult the physician as clinically indicated.
- Consider agranulocytosis and order a CBC with diff in any patient on clozapine presenting to health centre with fever, sore throat, or flu-like symptoms. A physician is to be consulted immediately if agranulocytosis is suspected.

Attending Psychiatrist:

- Initiating psychiatrist must ensure patient is registered with GenCAN registry.
- Order baseline and ongoing clozapine blood work and frequency at which the patient needs to be followed up by the CPN.
- Liaise with Akausisarvik mental health nurse and community psychiatric nurse regarding management of patients with severe lab abnormalities and non-compliance with clozapine regimen in a timely fashion.
- Inform GenCAN registry when patients re-start, titrate, or discontinue clozapine treatment.

Qikiqtani General Hospital Laboratory:

- Provide a weekly list of laboratory clozapine results to GenCAN.
- Ensure Akausisarvik Mental Health Nurse is made aware when standing orders for clozapine bloodwork is about to expire.

GenCAN Nurse Co-ordinator:

- Provide guidance to Akausisarvik mental health nurse regarding blood work schedule and managing minor lab abnormalities.
- Available 24/7 to give advice for emergencies related to clozapine.

EDUCATION

Clozapine is a medication that is commonly used for treatment-resistant schizophrenia. It takes an average of 6 months to determine effectiveness of treatment (range of 4-12 months). Suggested plasma levels are at least 350 ng/mL (1070 nmol/L), with no upper limit defined.

Clozapine may cause a rare but potentially serious complication called agranulocytosis (low white blood cell count). This can occur at any time after clozapine initiation. Patients on clozapine must be monitored regularly for agranulocytosis. Patients on clozapine who present with fever must be examined and worked up thoroughly to ensure their immune system is intact as they may be at risk for life-threatening infection.

Myocarditis, pericarditis and cardiomyopathy are all rare but serious complications of clozapine therapy. Myocarditis and pericarditis usually occur in the first 3 weeks of treatment with dose titration, in patients under 50 years. Early recognition is important due to high mortality rate.

Side Effects of Clozapine
<ul style="list-style-type: none"> • Hematologic: <ul style="list-style-type: none"> • leukopenia, neutropenia, agranulocytosis, leukocytosis, anemia, eosinophilia, thrombocytopenia, thrombocytemia • Cardiac: <ul style="list-style-type: none"> • tachycardia (25%), also pericarditis, myocarditis, cardiomyopathy • Central Nervous System: <ul style="list-style-type: none"> • Seizures (5% for doses of 600-900 mg) • Gastrointestinal: <ul style="list-style-type: none"> • nausea, gastro-esophageal reflux, hypomotility, ileus, obstruction, infarction • Neuropsychiatric: <ul style="list-style-type: none"> • sedation, dizziness, obsessive compulsive symptoms • Cardiovascular: <ul style="list-style-type: none"> • hypotension, tachycardia, dizziness, venous thromboembolism • Metabolic: <ul style="list-style-type: none"> • weight gain, diabetes, dyslipidemia • Other: <ul style="list-style-type: none"> • hypersalivation, enuresis

In Nunavut, the Gen-clozapine brand of clozapine (GenCAN/Mylan Canada) is used, in order to follow Nunavut patients through a single monitoring registry. All clozapine patients must be registered with GenCAN to ensure their white blood cell count remains in normal range. The GenCAN labs provide ongoing support regarding blood work monitoring for these patients.

PROCEDURE

1. Patients New to Clozapine Treatment:

1. A physician's order is required for the initiation of Clozapine treatment.
 - The physician assesses the patient and orders baseline blood work (CBC with differential) and provides direction to the nurse on when to consult the physician.
 - Prior to initiating treatment, the physician must ensure the WBC and ANC are within the acceptable range (see attached *Hematological Monitoring Guidelines - Green Status*).
 - Additional pre-treatment examinations: ECG, weight, blood pressure, pulse, fasting lipid profile and fasting serum glucose.
2. *GenCAN Patient Registration Form:*
 - The ordering physician completes sections 1 and 4 (see Sample Form for guidance).
 - The pharmacist will fax the completed form to GenCAN. Fax 1-800-497-9592. Phone 1-866-501-3338. www.gencan.ca.
3. The required standing blood work (CBC with differential) is ordered by the physician and the lab will fax these results to GenCAN.

2. Clozapine Monitoring

Each patient must be monitored for agranulocytosis with regular CBC with differential to be drawn according to the monitoring schedule. GenCAN will provide guidance about the most appropriate monitoring schedule. CBC is usually drawn weekly for first 26 weeks; then biweekly for 26 weeks; and every 4 weeks after 1 year of continuous treatment. The change in frequency is evaluated on an individual patient basis. Frequency becomes more frequent after interruption and re-initiation of clozapine. The best way to ensure blood work is regularly sent to the GenCAN registry is to add the registry as a CC on the original lab requisition. The healthcare team must troubleshoot management of problematic lab results (*see Hematological Monitoring Guidelines*) and patients who are noncompliant with the medication or blood work regimen.

Patients on clozapine should be monitored for side effects at each encounter. Most common side effects are constipation, weight gain, and tachycardia (see chart on page 4).

Clozapine Hematologic STOPLIGHT Criteria:

Patients on clozapine who present in the “yellow” range or who present with flu-like symptoms should be evaluated and have CBC monitored twice weekly.

Patients in the “red” range should have clozapine treatment discontinued, and CBC monitoring should continue as well as clinical evaluation for flu-like symptoms or other indicators of infection.



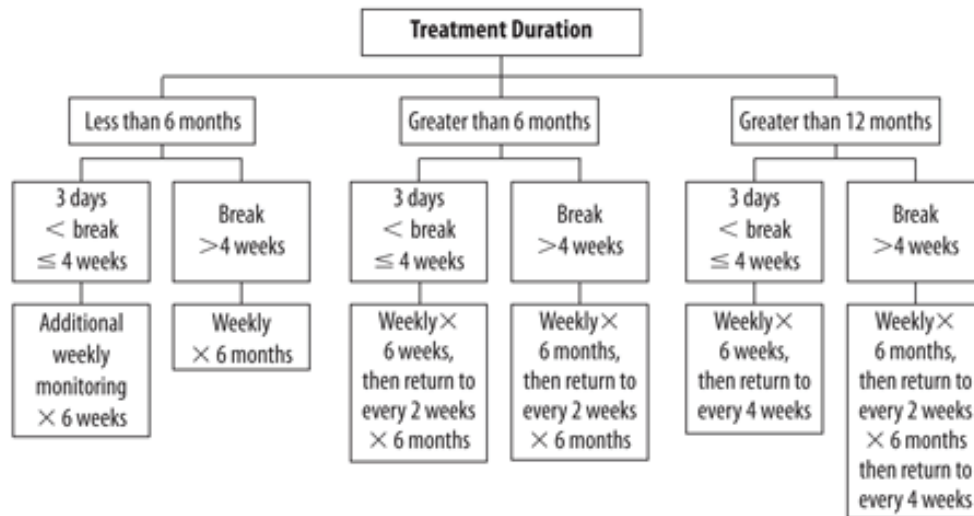
Patients on Clozapine who Present with Fever, Sore Throat, or Flu-like symptoms:

- Review date of previous clozapine bloodwork
- Clinical evaluation for other signs of infection
- Draw CBC to look for neutropenia
- Clinical evaluation for cardiovascular symptoms, including chest pain, arrhythmia, which may suggest myocarditis.
- Consider ECG and cardiac enzymes if cardiovascular symptoms are present

PRACTICE NOTE: The CPN must consult CHN, NP or MD for further evaluation and treatment if patient presents with fever, sore throat or flu-like symptoms.

Missed Doses

Contact attending psychiatrist for interruption of treatment for over 3 days. New orders must be obtained by attending psychiatrist for re-initiating treatment after missed clozapine doses or interruption of treatment. When therapy is re-initiated, more frequent blood work is required. A general guideline is found below. For further information see GenCAN UserGuide (reference 3).



ATTACHMENTS

1. GenCAN Patient Registration Form
2. GenCAN Blood Test Results Form
3. GenCAN Hematological Monitoring Guidelines
4. Sample GenCAN Patient Registration Form

REFERENCES

1. "Clozapine Treatment Protocol". The Credit Valley Hospital. 2006.
2. "Clozapine". LexiComp Database. Accessed June 2014.
3. GenCAN Userguide. www.GenCAN.ca. Accessed August 2014.

APPENDIX

CONTACTS

David Brannon, GenCAN Clinical Nurse Coordinator for Nunavut
1-866-781-7274 (available 24 hours)

Dr. Allison Crawford, Medical Director, Northern Psychiatric Outreach Program
Centre for Addiction and Mental Health
825-250 College St., Toronto, ON M5T 1R8
t. 416.535.8501 x30318 | f. 416.979.6902 | e. allison.crawford@utoronto.ca