CLOZARIL® (clozapine) tablet is indicated in the management of symptoms of treatment-resistant schizophrenia.[1]

CLOZARIL® is available only through the CLOZARIL® Support and Assistance Network® (CSAN®) distribution system that ensures weekly, every-two-week, or every-four-week hematological testing prior to the dispensing of the next period's supply of CLOZARIL®.[1]

Hematological quick reference chart[1]*

How CSAN® defines results associated with ANC† laboratory values[2]

Green (normal values for clozapine treatment)

- ANC ≥ 2.0 × 10^9/L
- BEN‡ Patient: ANC ≥ 1.0 x 10^9/L

- Continue to dispense CLOZARIL®
- Monitor as follows for eligible patients:§
  - Weekly for the first 26 weeks
  - Every 2 weeks for the next 26 weeks
  - Every 4 weeks as of 52 weeks

Yellow Alert(s)

ANC in the range of:
- ≥ 1.5 × 10^9/L < 2.0 × 10^9/L
- BEN Patient: ANC ≥ 0.5 to < 1.0 x 10^9/L

Particular attention should be paid if patient presents with the following: Any flu-like complaints or other symptoms that might suggest infection (i.e., fever, sore throat, or any other signs of infection).

- Hematological monitoring at least twice a week until ANC stabilize or increase
- Continue to dispense CLOZARIL®

Red Alert(s)

- ANC < 1.5 × 10^9/L
- BEN Patient: ANC < 0.5 x 10^9/L

Consider protective isolation when:
- ANC < 0.5 × 10^9/L

Should evidence of infection develop, appropriate cultures should be performed, and an appropriate antibiotic regimen be instituted.

Immediately withhold CLOZARIL® and monitor patient closely.

Confirmation of the hematological values is recommended within 24 h.

Stop CLOZARIL® therapy immediately if results are confirmed.

If the patient is discontinued due to neutropenia, monitoring should be conducted at least twice a week until ANC is normal (ANC is ≥ 2.0 x 10^9/L). BEN Patient: Monitor at least twice weekly until ANC ≥ 1.0 x 10^9/L.

Particular attention should be paid to any flu-like complaints or other symptoms which might suggest infection (i.e., fever, sore throat, or any other signs of infection).

A non-rechallengeable status is immediately assigned to the patient's profile for clozapine associated neutropenia.

CLOZARIL® therapy must not be resumed.

Consult with a CSAN® hematologist.

Additional evaluation may be needed to determine if baseline neutropenia is due to benign ethnic neutropenia (BEN). Consider hematology consultation before initiating or during CLOZARIL® treatment as necessary. Patients with BEN require a different ANC algorithm for CLOZARIL® management due to their lower baseline ANC levels.

*Please consult the CLOZARIL® Product Monograph for complete hematological monitoring information.

§The change from a weekly to a "once every two weeks" or from a "once every two weeks" to a "once every four weeks" schedule should be based upon the hematological profile of the patient, the clinical judgement of the treating physician, and if deemed appropriate, a consulting hematologist, as well as the patient's willingness to pursue a given frequency of blood monitoring.

The clinical evaluation should take into consideration possible factors that would place the patient in a higher risk group. Weekly hematological testing should be resumed for an additional 6 weeks if therapy is disrupted for more than 3 days. If clozapine is interrupted for 4 weeks or longer, weekly monitoring is required for an additional 26 weeks.

Please consult the CLOZARIL® Product Monograph at https://www.hlstherapeutics.com/wp-content/uploads/monograph_pdf/HLS-Clozaril-PM-E.pdf for important information about:

- Contraindications in patients with myeloproliferative disorders, a history of toxic or idiosyncratic agranulocytosis or severe granulocytopenia (with the exception of granulocytopenia/agranulocytosis from previous chemotherapy). [Clozapine should not be used simultaneously with other agents known to suppress bone marrow function]; in patients with active liver disease associated with nausea, anorexia, or jaundice; progressive live disease; and hepatic failure; in patients unable to undergo blood tests; severe central nervous system depression or comatose states, severe renal or cardiac disease (e.g., myocarditis), paralytic ileus, uncontrolled epilepsy.
- The most serious warnings and precautions regarding severe neutropenia (agranulocytosis), myocarditis and cardiomyopathy and mitral valve incompetence, and increased mortality in elderly patients with dementia.
- Other relevant warnings and precautions regarding neutropenia, fever, anticholinergic activity, rebound, withdrawal effects, cardiotoxicity and other adverse cardiovascular and respiratory effects, QT interval prolongation, venous thromboembolism, driving and operating machinery, metabolic changes, hyperglycemia, dyslipidemia, weight gain, priapism, severe neutropenia, eosinophilia, thrombocytopenia, hepatotoxicity, hepatic impairment, seizures, falls, neuroleptic malignant syndrome, tardive dyskinesia, renal impairment, severe cutaneous adverse reactions, pregnant and breast-feeding women, routine monitoring of liver function tests, should not be used for elderly patients with dementia, and caution in patients at risk for aspiration pneumonia.
- Conditions of clinical use, adverse reactions, drug interactions and dosing instructions.

The Product Monograph is also available by calling 1-800-267-2726.

Questions?

Don't hesitate to contact us:

CSAN®

Phone: 1-800-267-2726

Fax: 1-800-465-1312

†ANC=absolute neutrophil count.
‡BEN=benign ethnic neutropenia.

References: 1. CLOZARIL® Product Monograph, HLS Therapeutics Inc., May 31, 2022. **2.** HLS Therapeutics Inc. Data on file. January 23, 2023.

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November 2023 CA-CL-00105-EN