CLOZARIL®

(clozapine) is used for the management of symptoms in treatment-resistant schizophrenia (TRS) patients.[1]

CSAN®

was designed to help them throughout their treatment journey.

CLOZARIL® Clozapine

CSAN®
PrCLOZARIL® (clozapine)
SUPPORT AND ASSISTANCE NETWORK

TRS & Guidelines

Who is your treatment-resistant patient?[2]

Antipsychotic trial 1	**Oral AP:** At least 6 weeks at the midpoint or greater of the licensed therapeutic dose range **LAI AP:** At least 6 weeks following reaching steady state
Antipsychotic trial 2	**Oral AP:** At least 6 weeks at the midpoint or greater of the licensed therapeutic dose range **LAI AP:** At least 6 weeks following reaching steady state
Antipsychotic **treatment-resistant schizophrenia** (TRS) is defined as: Persistence of **2 or more positive symptoms** with at least a **moderate level of severity**, or a **single positive symptom with severe or greater severity**, following **2 or more adequate trials** with different antipsychotic drugs	
Clozapine trial	At least 8, but preferably 12, weeks at a dose of ≥400 mg/day; where available, obtaining trough levels ≥350 ng/mL (1,100 nM/L) for once-a-day dosing and ≥250 ng/mL for equally divided dosing are suggested
Following an adequate trial with clozapine, if the criteria above continue to be met, the specifier “clozapine-resistant schizophrenia” should be added.	

~25%-30% of patients with schizophrenia meet the criteria for **TRS**[2]

The Canadian Schizophrenia Guidelines cites that established guidelines have identified clozapine as the only indicated treatment in TRS.[2]

Recommendation 1:	Recommendation 2:
Clozapine should be offered to patients who have TRS. (Grade A recommendation)*	Clozapine should be considered for patients whose schizophrenia has not responded to 2 antipsychotics. (Grade B recommendation)†

Please refer to the Canadian Schizophrenia Guidelines for complete information.

CLOZARIL® (clozapine) tablet is indicated in the management of symptoms of treatment-resistant schizophrenia. In controlled clinical trials, clozapine was found to improve both positive and negative symptoms.[1]

AP: antipsychotic; **LAI:** long-acting injection.

*Grade A recommendation: At least one meta-analysis, systematic review, or randomized controlled trial rated as “1++” and directly applicable to the target population or a body of evidence consisting principally of studies rated as “1+”, being directly applicable to the target population, and demonstrating overall consistency of results.

†Grade B recommendation: A body of evidence including studies rated as “2++”, being directly applicable to the target population, and demonstrating overall consistency of results or extrapolated evidence from studies rated as “1++” or “1+”.

1++: High-quality meta-analyses, systematic reviews of randomized controlled trials, or randomized controlled trials with a very low risk of bias.

1+: Well-conducted meta-analyses, systematic reviews, or randomized controlled trials with a low risk of bias.

2++: High-quality systematic reviews of case control or cohort studies or high-quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal.

CLOZARIL® treatment protocol quick reference[1]

		Patients starting CLOZARIL® treatment	Patient resuming CLOZARIL® after interruption in therapy
Prescriber			**Do not resume in:** • Patients who have been discontinued due to clozapine-associated neutropenia (ANC <1.5 x 10^9/L, i.e., non-rechallengeable status) • Patients with clozapine-induced myocarditis
	Physical examination	Ensure no contraindications.	Ensure no contraindications.
	Cardiac evaluation	In patients with a family history of heart failure.	Ensure no contraindications. If patient has previously experienced **respiratory or cardiac arrest** with initial dosing but was then able to be successfully titrated to a therapeutic dose, re-titrate with extreme caution after even 24 hours of discontinuation.
	Informed consent	Consent to participate in the CLOZARIL® Support and Assistance Network (CSAN®).	
	Complete blood count (CBC)	Required: Baseline CBC Provide patient with a standing lab requisition for a weekly CBC with differential.	Required: New baseline CBC Provide patient with a standing lab requisition for a CBC with differential based on blood monitoring frequency.
	Other clinical monitoring	Baseline and periodic follow-up: Blood glucose, lipid profile, and body weight/BMI	
	Other considerations		**Restarting patients after 2 or more days since last dose:** Re-initiate with 12.5 mg once or twice on first day. If well tolerated, it may be feasible to titrate patient back to a therapeutic dose more quickly than recommended for initial treatment. **Restarting patients after 3 or more days since last dose:** Weekly hematological testing should be resumed for an additional 6 weeks.
	CSAN® registration/update	Consent must be obtained from all CLOZARIL® patients. Registration of the patient, their current location, treating physician, testing laboratory and dispensing pharmacist in the CSAN® system is also required. Request a form via fax by calling CSAN® at 1-800-267-2726 OR Download the CSAN® form from **HERE** to enroll your patients.	
		Complete section 4. Treatment initiation follows registration.	Complete section 4 to update the prescriber.

For additional details, please refer to the CLOZARIL® Product Monograph.
CSAN®-experienced consultants are also available at 1-800-267-2726 to assist you with any questions.

Pharmacist

CLOZARIL® treatment protocol quick reference[1]

		Patients starting CLOZARIL® treatment	Patient resuming CLOZARIL® after interruption in therapy
Pharmacist	**CLOZARIL® dispensing**	Upon confirmation that hematological monitoring has been conducted for the current period, dispense to the patient a supply of CLOZARIL® on a **weekly, every-two-week,** or **every-four-week** basis.	
	Clozapine brands	Patients may not be switched from one brand of clozapine to another without the completion of a new registry-specific patient registration form signed by the prescribing physician.	
	CSAN® registration/update	Consent must be obtained from all CLOZARIL® patients. Registration of the patient, their current location, treating physician, testing laboratory and dispensing pharmacist in the CSAN® system is also required. Request a form via fax by calling CSAN® at 1-800-267-2726 OR Download the CSAN® form from **HERE** to enroll your patients. Complete section 3.	

For additional details, please refer to the CLOZARIL® Product Monograph.
CSAN®-experienced consultants are also available at 1-800-267-2726 to assist you with any questions.

Prescriber

Hematological test results are readily available with CSAN® Pronto®

CLOZARIL® is available only through the 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]

CSAN PRONTO
®CLOZARIL® (clozapine) SUPPORT AND ASSISTANCE NETWORK

A capillary point-of-care device that generates results in real-time and simultaneously auto-uploads them to the patient's CSAN® profile

Hematological quick reference chart[1]

How CSAN® defines results associated with ANC laboratory values[3]

Green (normal values for clozapine treatment)

Yellow Alert(s)

Red Alert(s)

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.

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Hematological quick reference chart[1]

How CSAN® defines results associated with ANC laboratory values[3]

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)

Red Alert(s)

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.

ANC: absolute neutrophil count.
BEN: benign ethnic neutropenia.

*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
- a consulting hematologist (if deemed appropriate)
- 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.

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Hematological quick reference chart[1]

How CSAN® defines results associated with ANC laboratory values[3]

Green (normal values for clozapine treatment)

Yellow Alert(s)

ANC in the range of:
- ≥1.5 × 10^9/L to <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 absolute neutrophil counts (ANC) stabilize or increase
- Continue to dispense CLOZARIL®

Red Alert(s)

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.

ANC: absolute neutrophil count.
BEN: benign ethnic neutropenia.

Hematological test results are readily available with CSAN® Pronto®

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Hematological quick reference chart[1]

How CSAN® defines results associated with ANC laboratory values[3]

Green (normal values for clozapine treatment)	
Yellow Alert(s)	
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 (≥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.

ANC: absolute neutrophil count.
BEN: benign ethnic neutropenia.

How to resume hematological monitoring frequency in the event of interruption in therapy greater than 3 days[1]

Duration of Treatment Prior to Interruption					
Less than 6 months		**6 to 12 months**		**Greater than 12 months**	
Interruption greater than 3 days, 4 or less weeks	Interruption greater than 4 weeks	Interruption greater than 3 days, 4 or less weeks	Interruption greater than 4 weeks	Interruption greater than 3 days, 4 or less weeks	Interruption greater than 4 weeks
Additional weekly monitoring x 6 weeks	Weekly monitoring x 6 months	Weekly monitoring x 6 weeks, then return to every 2 weeks x 6 months	Weekly monitoring x 6 months, then return to every 2 weeks x 6 months	Weekly monitoring x 6 weeks, then return to every 4 weeks	Weekly monitoring x 6 months, then every 2 weeks x 6 months, then every 4 weeks

- Monitoring must continue for as long as the patient is on the drug.
- Monitoring frequency does not have to be modified if therapy is interrupted for 3 days or less.

Clozapine can be used only if regular hematological examinations can be guaranteed. This requires:

- The physician must obtain consent from all patients taking clozapine.
- Registration of the patient, their current location, treating physician, testing laboratory and dispensing pharmacist in the CSAN® system.
- Maintenance of a national HLS Therapeutics Inc. monitoring system of the hematological results of all patients on CLOZARIL® and provides timely feedback (within 24 hours of receipt of the blood test results) to the treating physician and dispensing pharmacist/or pharmacy
- The ability to identify patients who have been assigned "Non-rechallengeable Status". This requires that HLS Therapeutics Inc. both provide to, and obtain from, all other approved suppliers† of clozapine, the Non-rechallengeable Status/Hematological Status of all patients. HLS Therapeutics Inc. must be able to provide this information within 24 hours of receiving a written request.

Physicians should not prescribe CLOZARIL® until the non-rechallengeable status and the hematological status of the patient have been verified.

For the distribution system to be effective, treating physicians must ensure that the hematological testing is performed at the required frequency and that arrangements are made for the hematological results to be sent to CSAN®. Physicians may obtain details on the CSAN® distribution system by calling a toll-free phone number 1 (800) 267-2726.

Other monitoring and distribution systems

Between 1991 and 2003, clozapine was distributed by a single manufacturer, and patients were monitored by this manufacturer's specific registry and distribution system. The introduction of clozapine from other manufacturers has now resulted in the establishment of manufacturer-specific registry and distribution systems. In order to ensure the safe use and continued monitoring of all patients taking clozapine, the physician must have obtained consent from the patient for the potential sharing of hematological and other safety data between clozapine registries.

Patients may not be switched from one brand of clozapine to another without the completion of a new registry-specific patient registration form signed by the prescribing physician.
If a patient is switched from one brand of clozapine to another, the frequency of hematological monitoring may continue unaltered unless a change is clinically indicated.

†"Approved supplier" is a manufacturer who holds a valid Notice of Compliance (NOC) for clozapine.

Recommended dosing and titration[1]

Day 1	12.5 mg O.D. or B.I.D.	Cautious titration and a divided dosage schedule are necessary to minimize the risks of hypotension, seizure, and sedation
Day 2	25 mg O.D. or B.I.D.	
Weeks 1-2	25-50 mg/day increases	If well tolerated, titrate upward in 25-50 mg daily increments
	Target 300-450 mg/day	If well tolerated, target 300-450 mg/day by the end of week 2 Subsequent dosage increases should be made no more than once or twice weekly in increments not to exceed 100 mg
Therapeutic dose range	300-600 mg/day in divided doses	In most patients, antipsychotic efficacy can be expected within the therapeutic range of 300-600 mg/day in divided doses The total daily dose may be divided unevenly, with the larger portion at bedtime
Since improvement may be gradual, continued therapeutic response can be expected beyond the first month of treatment.		
Maximum dose	600-900 mg/day **Maximum dose of 900 mg/day should not be exceeded**	Doses up to 900 mg/day may be required to obtain an acceptable therapeutic response Patients must be given adequate time to respond to a given dose level before escalation to a higher dose Note: An increase in adverse reactions (particularly seizures) at daily doses ≥600 mg may occur
Maintenance	Gradually decrease to target	After achieving maximum therapeutic benefit, many patients can be maintained effectively at lower doses At daily doses not exceeding 200 mg, a single administration in the evening may be appropriate Patients should be periodically reassessed to determine the continued need for maintenance treatment
	Target 150-300 mg/day in divided doses	

CLOZARIL® should be initiated once the neuroleptic is completely discontinued for at least 24 hours. CLOZARIL® should not be used in combination with other neuroleptics.

Patients 60 years of age and older: It is recommended that treatment in patients 60 years and older is initiated at a particularly low dose of CLOZARIL® (12.5 mg given once on the first day) with subsequent dose increments restricted to 25 mg/day.

Cardiovascular disorders: Severe cardiovascular disorders are contraindications. CLOZARIL® should be used with caution in patients with known cardiovascular and/or pulmonary disease, particularly in those with cardiac arrhythmias and conduction disturbances, and the recommendation for gradual titration of dose should be carefully observed.

Renal impairment: In patients with mild to moderate renal impairment the initial dose of CLOZARIL® should be 12.5 mg given once on the first day, and dosage increase should be slow and in small increments.

Hepatic impairment: Patients with hepatic impairment should receive CLOZARIL® with caution along with regular monitoring of liver function tests.

Please refer to the CLOZARIL® Product Monograph for complete dosing and administration information.

Adverse drug reactions[1]

The most serious adverse reactions experienced with CLOZARIL® were neutropenia, seizure, cardiovascular effects and fever.

Treatment-emergent adverse events occurring in ≥5% of patients taking clozapine in clinical trials		% Patients (N=842)
Adverse Event	**Nervous system disorders**	Drowsiness/sedation: 39
		Dizziness/vertigo: 19
		Headache: 7
		Tremor: 6
	Cardiac disorders	Tachycardia: 25*
	Vascular disorders	Syncope: 6
		Hypotension: 9
	Gastrointestinal disorders	Constipation: 14
		Nausea: 5
		Dry mouth: 6
	Autonomic nervous system	Salivation: 31
		Sweating: 6
		Visual disturbances: 5
	Miscellaneous	Fever: 5

*Rate based on population of approximately 1700 exposed during premarket clinical evaluation of clozapine.
Adapted from the CLOZARIL® Product Monograph.

Important safety information

Indication and clinical use not mentioned elsewhere:

- CLOZARIL® (clozapine) is indicated in the management of symptoms of treatment-resistant schizophrenia. In controlled clinical trials, clozapine was found to improve both positive and negative symptoms.
- Due to the significant risk of neutropenia and seizure associated with its use, clozapine should be limited to treatment-resistant schizophrenic patients who are non-responsive to, or intolerant of, conventional antipsychotic drugs. Non-responsiveness is defined as the lack of satisfactory clinical response, despite treatment with appropriate courses of at least two marketed chemically-unrelated antipsychotic drugs. Intolerance is defined as the inability to achieve adequate benefit with conventional antipsychotic drugs because of dose-limiting, intolerable adverse effects.
- Because of the significant risk of neutropenia and seizure, events which both present a continuing risk over time, the extended treatment of patients failing to show an acceptable level of clinical response to clozapine should ordinarily be avoided. Seizure risk is dose-related and is more likely to occur with rapid dose increases. Titrate gradually and use divided doses. Use with caution in patients with history of seizure or risk factors for seizure.
- Can be used only if regular hematological examinations through CSAN® can be guaranteed.
- Should not be prescribed until the non-rechallengeable status and the hematological status of the patient have been verified.
- Consent from the patient for the potential sharing of hematological and other safety data between clozapine registries must be obtained.
- Completion of a new registry-specific patient registration form signed by the prescribing physician for patients switching from one brand of clozapine to another.
- Not indicated in pediatrics (<18 years of age).
- Use with care in the elderly (>60 years of age).

Contraindications:

- 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
- Active liver disease associated with nausea, anorexia, or jaundice; progressive liver disease; hepatic failure
- Patients unable to undergo routine blood tests
- Severe central nervous system depression or comatose states
- Severe renal or cardiac disease (e.g., myocarditis)
- Paralytic ileus
- Uncontrolled epilepsy

Most serious warnings and precautions:

Severe Neutropenia (Agranulocytosis): CLOZARIL® treatment has caused severe neutropenia, defined as an absolute neutrophil count (ANC) less than 0.5 x 10^9/L. Severe neutropenia can lead to serious infection and death. Prior to initiating treatment with CLOZARIL® a baseline ANC must be at least ≥2.0 x 10^9/L for the general population; and must be at least ≥1.0 x 10^9/L for patients with documented Benign Ethnic Neutropenia (BEN). Regular hematologic monitoring is required prior to dispensing, because of the significant risk of this potentially life-threatening adverse event. Advise patients to immediately report the appearance of lethargy, weakness, fever, sore throat, flu-like complaints or any other signs of infection. Because of the risk of severe neutropenia, CLOZARIL® is available only through a distribution system ("CSAN") that ensures weekly, every-two-week or every-four-week hematological testing prior to the dispensing of the next period's supply of CLOZARIL®.

Myocarditis, Pericarditis, and Cardiomyopathy and Mitral Valve Incompetence: Fatal myocarditis and cardiomyopathy have occurred with the use of CLOZARIL®. Discontinue CLOZARIL® and obtain a cardiac evaluation upon suspicion of myocarditis, pericarditis, or cardiomyopathy. Consider the possibility of myocarditis or cardiomyopathy if chest pain, tachycardia, palpitations, dyspnea, fever, flu-like symptoms, hypotension, or ECG changes occur. Generally, patients with a history of clozapine-associated myocarditis or cardiomyopathy should not be rechallenged with CLOZARIL®.

Increased Mortality in Elderly Patients with Dementia: Elderly patients with dementia treated with antipsychotic drugs are at an increased risk of death compared to those treated with placebo. CLOZARIL® is not approved for use in elderly patients with dementia.

Other relevant warnings and precautions:

- Risk of fever, possibility of an underlying infectious process or the development of blood dyscrasia
- Anticholinergic activity, caution in the presence of prostatic enlargement, narrow-angle glaucoma or paralytic ileus. Monitor for early onset of constipation
- Rebound/withdrawal effects
- Other adverse cardiovascular and respiratory effects
- QT interval prolongation
- Venous thromboembolism
- Driving and operating machinery
- Metabolic changes (hyperglycemia, dyslipidemia, and body weight gain); monitor blood glucose, body weight and lipid evaluations
- Priapism
- Eosinophilia
- Thrombocytopenia: Discontinue CLOZARIL® if platelet count falls below 50.0 x 10^9/L
- Hepatotoxicity: Monitor for signs and symptoms of hepatotoxicity, and serum test for liver injury. Permanently discontinue CLOZARIL® if hepatitis or transaminase elevations combined with other systemic symptoms are due to clozapine
- Hepatic impairment: Regular liver function tests (LFTs). Discontinue CLOZARIL® if LFTs are elevated or symptoms of jaundice occur
- Seizures
- Falls
- Neuroleptic malignant syndrome
- Tardive dyskinesia
- Renal impairment
- Severe cutaneous adverse reactions (SCARs): Stevens-Johnson syndrome, toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), and acute generalized exanthematous pustulosis (AGEP); discontinue CLOZARIL® if SCAR occurs
- Pregnant women: To monitor outcomes in women exposed to CLOZARIL® during pregnancy, patients and healthcare professionals are encouraged to report a pregnancy by calling the CLOZARIL® Support and Assistance Network® (CSAN®) at 1 (800) 267-2726.
- Women of childbearing potential and contraceptive measures
- Breastfeeding women
- Should not be used for elderly patients with dementia
- Caution in patients at risk for aspiration pneumonia
- Cerebrovascular adverse events (including stroke) in elderly patients with dementia)
- Concomitant administration of drugs known to inhibit or induce the activity of cytochrome P450 isozymes

For more information:

Please consult the CLOZARIL® Product Monograph at **http://www.hlstherapeutics.com/wp-content/uploads/monograph_pdf/HLS-Clozaril-PM-E.pdf** for important information on adverse reactions, drug interactions (particularly CYP 450 isoenzymes inhibitors or inducers drugs), and dosing information (including certain clinical situations where monitoring for elevated clozapine blood levels may be advised) which have not been discussed in this piece. The Product Monograph is also available by calling 1-800-267-2726.

Tailored services supported by a team of experts to help optimize patient management

- Supporting you **24/7/365** (including holidays) with any required assistance – including use of the CSAN® Patient Care Portal
- Access to **bilingual specialty consultants** who can help guide a unique course of action throughout your patient's CLOZARIL® treatment journey:
  - Psychiatrists, cardiologists, registered nurse educators, a hematologist, and a nutritionist
- **CSAN® Pronto®:** A **capillary point-of-care device** designed to enhance the mandatory safety blood monitoring requirement for patients prescribed CLOZARIL®
  - To help simplify routing hematological monitoring required for patients treated with CLOZARIL®, CSAN® Pronto® offers onsite testing and can generate white blood cell counts/neutrophil percentage from a drop of capillary-drawn blood.
  - Results are automatically uploaded into the CSAN® Patient Care Portal and made available to the healthcare team within minutes for added convenience.
- **Lablink+:** A bidirectional interface, which allows blood test results to flow electronically between CSAN® and hospital information systems
- Travel assistance service
- Benign ethnic neutropenia (BEN) protocol

FOR QUESTIONS AND INQUIRIES, CALL CSAN® AT: 1-800-267-2726

References:

1. CLOZARIL® Product Monograph, HLS Therapeutics Inc. July 10, 2025.
2. Remington G, *et al*. Guidelines for the pharmacotherapy of schizophrenia in adults. *Can J Psychiatry*. 2017;62(9):604-616.
3. HLS Therapeutics Inc. Data on file. Jan. 23, 2023.

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