



# CLOZARIL: Starting a Patient

1. Call the CLOZARIL National Registry (CNR) to obtain a rechallenge number and to confirm that you and your pharmacy are registered.
2. Obtain a baseline WBC with differential from patient. If within normal limits, WBC  $\geq 3500/\text{mm}^3$ , ANC  $\geq 1500/\text{mm}^3$ , prescribe CLOZARIL tablets.
3. Submit WBC information to the registered pharmacy.
4. Please be prepared to provide your DEA # to the CNR when you are registering for the first time.

**For forms, patient enrollment, or medical information call the CLOZARIL National Registry:  
1-800-448-5938**

## Recommended CLOZARIL® (clozapine) dosage titration at start of therapy<sup>1</sup>

Week 1	am (mg)	hs (mg)	Total (mg)	Week 2	am (mg)	hs (mg)	Total (mg)
Day 1	12.5	12.5*	12.5-25	Day 8	50	100	150
Day 2	25	—	25	Day 9	100	100	200
Day 3	25	25	50	Day 10	100	100	200
Day 4	25	50	75	Day 11	50	200	250
Day 5	50	50	100	Day 12	50	200	250
Day 6	50	75	125	Day 13	100	200	300
Day 7	50	100	150	Day 14	100	200	300

\*Optional  
Subsequent dosage increments should be made no more than once or twice weekly, in increments not to exceed 100 mg.

CLOZARIL® (clozapine) use is associated with a substantial risk of seizure, affecting 1% to 2% of patients at low doses (below 300 mg/day), 3% to 4% at moderate doses (300 mg/day to 600 mg/day), and 5% at high doses (600 mg/day to 900 mg/day). In clinical trials, CLOZARIL was associated with a 1% to 2% incidence of agranulocytosis, a potentially fatal blood disorder, which, if caught early, can be reversed. Mandatory monitoring of white blood cell counts and drug dispensing as per the requirements specified in the package insert, provide an efficient means of determining developing agranulocytosis. Analysis of post-marketing safety databases suggests that CLOZARIL is associated with an increased risk of fatal myocarditis, especially during, but not limited to, the first month of therapy. Orthostatic hypotension may occur in some patients, especially during the initial phases of treatment, and can, in rare cases (approximate incidence of 1/3,000), be accompanied by collapse and/or cardiac arrest.

**References:** 1. Meltzer HY. Treatment of the neuroleptic-nonresponsive schizophrenic patient. *Schizophr Bull.* 1992;18(3):515-542.  
2. CLOZARIL Prescribing Information. Novartis Pharmaceuticals Corporation.

## NEW INDICATION

In schizophrenia and schizoaffective disorder

**Clozaril®**  
(clozapine) 

**Proven To Reduce  
Recurrent Suicidal Behavior**

# Leukopenia, Granulocytopenia, and Agranulocytosis: Definitions and Suggested Clinical Management<sup>2</sup>

Problem phase	WBC* or ANC* per mm <sup>3</sup>	Clinical findings	Suggested clinical management
Mild Leukopenia	WBC 3000-3500	Monitor closely for clinical symptoms, such as: lethargy, fever, sore throat, or weakness	<ol style="list-style-type: none"> <li>1. Monitor patient closely</li> <li>2. Twice-weekly WBC tests with differentials should be performed</li> <li>3. CLOZARIL® (clozapine) therapy may continue</li> <li>4. Treat infections appropriately</li> </ol>
Moderate Leukopenia or Moderate Granulocytopenia	WBC 2000-3000 or ANC 1000-1500	Monitor closely for clinical symptoms, such as: lethargy, fever, sore throat, or weakness	<ol style="list-style-type: none"> <li>1. Interrupt CLOZARIL at once and notify CNR* (800-448-5938)</li> <li>2. Institute WBC tests with differentials every day until WBC count &gt;3000/mm<sup>3</sup> and ANC &gt;1500/mm<sup>3</sup>; then perform twice weekly WBC and differential counts until WBC count ≥3500/mm<sup>3</sup></li> <li>3. Treat infections appropriately</li> <li>4. CLOZARIL therapy may be reinstated (with twice-weekly monitoring) when WBC &gt;3000/mm<sup>3</sup> and ANC &gt;1500/mm<sup>3</sup>, and no symptoms of infection are present</li> <li>5. Once WBC count ≥3500/mm<sup>3</sup> patient must be followed weekly for 6 months without any leukopenia; then patient may go to biweekly WBC monitoring</li> </ol>
Severe Leukopenia or Severe Granulocytopenia	WBC below 2000 or ANC 500-1000	Monitor closely for clinical symptoms, such as: lethargy, fever, sore throat, or weakness	<ol style="list-style-type: none"> <li>1. <b>Discontinue CLOZARIL at once and notify CNR* (800-448-5938)</b></li> <li>2. <b>Consult with a hematologist for current treatment options</b></li> <li>3. <b>Treat infections aggressively</b></li> <li>4. <b>Monitor patient daily until WBC and differential counts return to normal (WBC ≥3500/mm<sup>3</sup> and ANC ≥1500/mm<sup>3</sup>), usually in about 2 weeks</b></li> <li>5. <b>CLOZARIL must <u>not</u> be restarted</b></li> <li>6. <b>Perform WBC tests for at least 4 weeks following discontinuation</b></li> </ol>
Agranulocytosis	ANC below 500	Evidence of a local infection (sore throat, skin, nail, or tooth abscess) or systemic infection (fever, lethargy, weakness, malaise) represents a medical emergency	<ol style="list-style-type: none"> <li>1. <b>Discontinue CLOZARIL at once and notify CNR* (800-448-5938)</b></li> <li>2. <b>Consult with hematologist or other specialist to determine appropriate treatment regimen</b></li> <li>3. <b>Treat infections aggressively</b></li> <li>4. <b>Consider admission for symptomatic agranulocytosis</b></li> <li>5. <b>Consider treating patient with a G-CSF/GM-CSF* drug until ANC &gt;1000/mm<sup>3</sup></b></li> <li>6. <b>Monitor patient daily until WBC ≥3500/mm<sup>3</sup> and ANC ≥1500/mm<sup>3</sup></b></li> <li>7. <b>CLOZARIL must <u>not</u> be restarted</b></li> <li>8. <b>Perform WBC tests for at least 4 weeks following discontinuation</b></li> </ol>

\*WBC = white blood cell count; ANC = absolute neutrophil count; CNR = CLOZARIL National Registry; G-CSF and GM-CSF = bone marrow colony-stimulating factors.

Please see accompanying full prescribing information.

