Required hematological monitoring with clozapine

There are two separate monitoring guidelines

- One for the general population
- Another for patients with benign ethnic neutropenia
  - Benign ethnic neutropenia (BEN) is a condition observed in certain ethnic groups whose average ANC values are lower than “standard” laboratory ranges for neutrophils.
  - It is most commonly observed in individuals of African descent (approximate prevalence of 25-50 percent), some Middle Eastern ethnic groups, and in other non-Caucasian ethnic groups with darker skin.
  - BEN is more common in men.
  - Patients with BEN have normal hematopoietic stem-cell number and myeloid maturation, are healthy, and do not suffer from repeated or severe infections.
  - Patients with BEN are not at increased risk for developing clozapine-induced neutropenia.
  - Additional evaluation may be needed to determine if baseline neutropenia is due to BEN.

Monitoring guidelines are presented here:
### Clozapine Absolute Neutrophil Count (ANC) Monitoring for the General Patient Population

<table>
<thead>
<tr>
<th>ANC Level</th>
<th>CLOZAPINE Treatment Recommendations</th>
<th>ANC Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal range (≥1500/µL)</td>
<td>☐ May initiate treatment or continue ongoing treatment ☐ If treatment interrupted: - &lt; 30 days, continue monitoring as before - ≥ 30 days, monitor as if new patient</td>
<td>☐ Weekly from initiation to 6 months ☐ Every 2 weeks from 6 to 12 months ☐ Monthly after 12 months</td>
</tr>
<tr>
<td>Mild Neutropenia (1000 to 1499/µL)*</td>
<td>☐ Continue treatment</td>
<td>☐ Three times weekly until ANC ≥1500/µL ☐ Once ANC ≥1500/µL, return to patient’s last “Normal Range” ANC monitoring interval**</td>
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<tr>
<td>Moderate Neutropenia (500 to 999/µL)*</td>
<td>☐ Recommend hematology consultation ☐ Interrupt treatment for suspected clozapine induced neutropenia ☐ Resume treatment once ANC ≥1000/µL</td>
<td>☐ Daily until ANC ≥1000/µL, then ☐ Three times weekly until ☐ ANC ≥1500/µL ☐ Once ANC ≥1500/µL, check ANC weekly for 4 weeks, then return to patient’s last “Normal Range” ANC monitoring interval**</td>
</tr>
</tbody>
</table>
| Severe Neutropenia (less than 500/µL)* | ☐ Recommend hematology consultation ☐ Interrupt treatment for suspected clozapine-induced neutropenia ☐ Do not rechallenge unless prescriber determines benefits outweigh risks | ☐ Daily until ANC ≥1000/µL, then ☐ Three times weekly until ANC ≥1500/µL ☐ If patient rechallenged, resume treatment as a new patient under “Normal Range” monitoring once ANC ≥1500/µL **
For Patients with Benign Ethnic Neutropenia (BEN)

<table>
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<tr>
<th>ANC Level</th>
<th>Treatment Recommendations</th>
<th>ANC Monitoring</th>
</tr>
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</table>
| Normal BEN Range (Established ANC baseline ≥1000/µL) | • Obtain at least two baseline ANC levels before initiating treatment  
• May continue ongoing treatment  
• If treatment interrupted  
  - < 30 days, continue monitoring as before  
  - ≥ 30 days, monitor as if new patient | ☑ Weekly from initiation to 6 months  
☑ Every 2 weeks from 6 to 12 months  
☑ Monthly after 12 months |
| BEN Neutropenia 500 to 999/µL* | • Recommend hematology consultation  
• Continue treatment | ☑ Three times weekly until ANC ≥ 1000/µL or ≥ patient’s known baseline  
☑ Once ANC ≥ 1000/µL or at patient’s known baseline, check ANC weekly for 4 weeks, then return to patient’s last “Normal BEN Range” ANC monitoring interval.** |
| BEN Severe Neutropenia less than 500/µL* | • Recommend hematology consultation  
• Interrupt treatment for suspected clozapine-induced neutropenia  
• Do not rechallenge unless prescriber determines benefits outweigh risks | ☑ Daily until ANC ≥500/µL, then  
☑ Three times weekly until ANC ≥ patient’s baseline  
☑ If patient rechallenged, resume treatment as a new patient under “Normal Range” monitoring once ANC ≥1000/µL or at patient’s baseline |

* Confirm all initial reports of ANC less than 1500/µL with a repeat ANC measurement within 24 hours
** If clinically appropriate