RISK EVALUATION AND MITIGATION STRATEGY (REMS) Document

Clozapine Shared System REMS Program

I. Administrative Information
Initial Shared System REMS Approval: 09/2015
Most Recent Modification: 11/2021

II. REMS Goal
The goal of the Clozapine REMS Program is to mitigate the risk of severe neutropenia associated with the use of clozapine by:

1. Educating prescribers and pharmacists about the risk of severe neutropenia and appropriate monitoring requirements
2. Informing patients about the risk of severe neutropenia and appropriate monitoring requirements
3. Ensuring prescribers submit documentation that periodic monitoring of patients is performed to identify severe neutropenia
4. Ensuring the prescriber documents a risk-benefit assessment when ANC falls below the acceptable range as described in the Prescribing Information
5. Establishing long-term safety and safe use of clozapine by enrolling all patients who receive clozapine in the registry

III. REMS Requirements
Clozapine Applicants must ensure that healthcare providers, patients, pharmacies, and wholesalers-distributors comply with the following requirements:

1. Healthcare Providers who prescribe clozapine for outpatient use and/or initiate treatment for inpatients must:

   To become certified to prescribe
   
   1. Review the drug’s Prescribing Information.
   3. Successfully complete the Knowledge Assessment for Prescribers and submit it to the REMS Program.
   4. Enroll in the REMS Program by completing the Prescriber Enrollment Form.
<table>
<thead>
<tr>
<th>Before treatment initiation (first dose)</th>
<th>5. Counsel the patient on the risks associated with clozapine, including severe neutropenia, and the Clozapine REMS Program requirements including to report signs of infection using <em>A Guide for Patients and Caregivers: What You Need to Know about Clozapine and Neutropenia</em>. Provide a copy to the patient unless clinical judgment indicates that the patient’s adherence to the treatment regimen will be negatively impacted by providing the Guide.</th>
</tr>
</thead>
<tbody>
<tr>
<td>6. Assess the patient’s absolute neutrophil count (ANC). Document and submit the ANC to the REMS program using the <em>Patient Enrollment Form</em>.</td>
<td></td>
</tr>
<tr>
<td>7. Enroll the patient in the REMS Program by completing and submitting the <em>Patient Enrollment Form</em> to the REMS program.</td>
<td></td>
</tr>
<tr>
<td>During treatment; according to the monitoring frequency in the Prescribing Information</td>
<td>8. Assess the patient’s ANC and monitoring frequency.</td>
</tr>
<tr>
<td>9. For patients with an ANC that falls below the acceptable range: Assess the patient’s health status for appropriateness of continuing treatment.</td>
<td></td>
</tr>
<tr>
<td>During treatment, monthly</td>
<td>10. Document and submit the ANC results, the monitoring frequency, and appropriateness for continuing treatment to the REMS program using the <em>Patient Status Form</em>.</td>
</tr>
<tr>
<td>After treatment discontinuation; according to the monitoring frequency in the Prescribing Information</td>
<td>11. Assess the patient’s ANC. Document and submit the ANC results to the REMS program using the <em>Patient Status Form</em>.</td>
</tr>
</tbody>
</table>

### 2. Patients who are prescribed clozapine:

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>2. Get a blood test to check your neutrophil count.</td>
<td></td>
</tr>
<tr>
<td>3. Be enrolled in the REMS Program. Enrollment information will be provided to the REMS Program.</td>
<td></td>
</tr>
<tr>
<td>During treatment; as directed by your prescriber</td>
<td>4. Get a blood test to check your neutrophil count.</td>
</tr>
<tr>
<td>After treatment discontinuation; as directed by your prescriber</td>
<td>5. Get a blood test to check your neutrophil count.</td>
</tr>
</tbody>
</table>
3. **Pharmacies that dispense clozapine for outpatient use must:**

<table>
<thead>
<tr>
<th>To become certified to dispense</th>
<th>1. Designate an authorized representative to carry out the certification process and oversee implementation and compliance with the REMS program on behalf of the pharmacy.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3. Have the authorized representative successfully complete the <em>Knowledge Assessment for Pharmacies</em> and submit it to the REMS program.</td>
</tr>
<tr>
<td></td>
<td>4. Establish processes and procedures to verify an available, current ANC is within the acceptable range for patients enrolled but not authorized to receive the drug.</td>
</tr>
<tr>
<td></td>
<td>5. Have the authorized representative enroll in the REMS program by completing and submitting the <em>Outpatient Pharmacy Enrollment Form</em> to the REMS program.</td>
</tr>
<tr>
<td></td>
<td>6. Train all relevant staff involved in dispensing clozapine on the requirements of the REMS program using the <em>Clozapine and the Risk of Neutropenia: A Guide for Pharmacists</em>.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Before dispensing</th>
<th>7. Obtain authorization to dispense each prescription by contacting the REMS Program to verify that the patient is enrolled and authorized to receive drug.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>8. For patients enrolled but not authorized to receive clozapine: Verify an available, current ANC is within the acceptable range through the processes and procedures established as a requirement of the REMS Program, document and submit the ANC and the prescriber’s NPI to the REMS Program and obtain authorization to dispense each prescription by contacting the REMS program to verify the patient is now authorized to receive clozapine.</td>
</tr>
<tr>
<td></td>
<td>9. Report dosing information to the REMS Program.</td>
</tr>
</tbody>
</table>

| To maintain certification to dispense | 10. Have the new Authorized Representative enroll in the REMS Program by reviewing *Clozapine and the Risk of Neutropenia: A Guide for Pharmacists*, successfully completing the *Knowledge Assessment for Pharmacies* and the *Outpatient Pharmacy Enrollment Form* and submitting both to the REMS Program. |

<table>
<thead>
<tr>
<th>At all times</th>
<th>11. Not distribute, transfer, loan, or sell clozapine except to certified dispensers.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>12. Maintain records of staff training and that all processes and procedures are in place and are being followed.</td>
</tr>
</tbody>
</table>
13. Comply with audits carried out by the manufacturers or a third party acting on behalf of the manufacturers, to ensure that all processes and procedures are in place and are being followed.

### 4. Pharmacies that dispense clozapine for inpatient use must:

| To become certified to dispense | 1. Designate an authorized representative to carry out the certification process and oversee implementation and compliance with the REMS program, on behalf of the pharmacy. |
|  | 3. Have the authorized representative successfully complete the *Knowledge Assessment for Pharmacies* and submit it to the REMS program. |
|  | 4. Establish processes and procedures to verify an available, current ANC is within the acceptable range for patients enrolled but not authorized to receive clozapine. |
|  | 5. Have the authorized representative enroll in the REMS program by completing and submitting the *Inpatient Pharmacy Enrollment Form* to the REMS program. |
|  | 6. Train all relevant staff involved in dispensing clozapine on the requirements of the REMS program, using the *Clozapine and the Risk of Neutropenia: A Guide for Pharmacists*. |

| Before dispensing, first dose | 7. Obtain authorization to dispense by contacting the REMS Program to verify that the patient is enrolled and authorized to receive the drug. |
|  | 8. For patients enrolled but not authorized by the REMS Program to receive the drug: Verify an available, current ANC is within acceptable range through the processes and procedures established as a requirement of the REMS Program, document and submit the ANC to the REMS Program and obtain authorization to dispense each prescription by contacting the REMS program to verify the patient is now authorized to receive clozapine. |

| At discharge | 9. Dispense no more than a 7-days’ supply. |

| To maintain certification to dispense | 10. Have the new authorized representative enroll in the REMS Program by reviewing *Clozapine and the Risk of Neutropenia: A Guide for Pharmacists*, successfully completing the *Knowledge Assessment for Pharmacies* and the *Inpatient Pharmacy Enrollment Form* and submitting both to the REMS Program. |

| At all times | 11. Maintain records of staff training and that all processes and procedures are in place and are being followed. |
|  | 12. Not distribute, transfer, loan, or sell clozapine except to certified dispensers. |
13. Comply with audits carried out by the manufacturers or a third party acting on behalf of the manufacturers, to ensure that all processes and procedures are in place and are being followed.

5. Wholesalers-distributors that distribute clozapine must:

<table>
<thead>
<tr>
<th>To be able to distribute</th>
<th>1. Establish processes and procedures to ensure that the drug is distributed only to certified pharmacies.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2. Train all relevant staff involved in distribution on the requirements of the REMS program.</td>
</tr>
<tr>
<td>At all times</td>
<td>3. Distribute only to certified pharmacies.</td>
</tr>
<tr>
<td></td>
<td>4. Maintain records of drug distribution for all clozapine shipments.</td>
</tr>
<tr>
<td></td>
<td>5. Maintain records that all processes and procedures are in place and are being followed.</td>
</tr>
<tr>
<td></td>
<td>6. Comply with audits carried out by the manufacturers or a third party acting on behalf of the manufacturers, to ensure that all processes and procedures are in place and are being followed.</td>
</tr>
</tbody>
</table>

Clozapine Applicants must provide training to healthcare providers who prescribe clozapine.

The training includes the following educational material: Clozapine and the Risk of Neutropenia: A Guide for Healthcare Providers and the Knowledge Assessment for Prescribers. The training must be available online and hardcopy format via mail by calling the REMS program.

Clozapine Applicants must provide training to pharmacies that dispense clozapine.

The training includes the following educational material: Clozapine and the Risk of Neutropenia: A Guide for Pharmacists and the Knowledge Assessment for Pharmacies. The training must be available online and hardcopy format via mail by calling the REMS program.

To inform healthcare providers about the REMS Program and the risks and safe use of clozapine, Clozapine Applicants must disseminate REMS communication materials according to the table below:

<table>
<thead>
<tr>
<th>Target Audience</th>
<th>Communication Materials &amp; Dissemination Plans</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prescribers certified in the Clozapine REMS</td>
<td>REMS Letter: Healthcare Provider Letter with attachment Factsheet: What's Changed in the Clozapine REMS for Prescribers?</td>
</tr>
<tr>
<td></td>
<td>1. Email within 30 calendar days of approval of the REMS modification, and again 30 calendar days later.</td>
</tr>
<tr>
<td></td>
<td>a. Send by mail or fax within 7 calendar days of the date the second email was sent if email was reported undeliverable or unopened.</td>
</tr>
<tr>
<td></td>
<td>2. Email within 90 calendar days of approval of the REMS modification and again 15 calendar days later.</td>
</tr>
<tr>
<td></td>
<td>a. Send by mail or fax within 7 calendar days of the date the second email was sent if email was reported undeliverable or unopened.</td>
</tr>
</tbody>
</table>

Reference ID: 4886777
<table>
<thead>
<tr>
<th>Target Audience</th>
<th>Communication Materials &amp; Dissemination Plans</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prescribers certified in the Clozapine REMS with 5 or more patients treated with Clozapine</td>
<td>Outbound Voice Call: Call beginning 30 calendar days after approval of the REMS modification and make up to 3 attempts within 90 calendar days.</td>
</tr>
</tbody>
</table>
| Prescribers not yet re-certified in the Clozapine REMS with 5 or more patients treated with Clozapine | Outbound Voice Call:  
1. Call beginning 120 calendar days after approval of the REMS modification and make 1 attempt within 30 calendar days.  
2. Call beginning 150 calendar days after approval of the REMS modification and make up to 2 attempts within 60 calendar days.                                                                                       |
| Healthcare providers who are likely to prescribe clozapine                      | REMS Letter: Healthcare Professional Society Letter with attachment Factsheet: What's Changed with the Clozapine REMS Program for Prescribers?, Drop In Summary for Healthcare Providers  
1. Disseminate within 15 calendar days of approval of the REMS modification through the following professional societies and request the letter or content be provided to their members:  
   a. American Society of Hematology, American Psychiatric Association  
   American College of Psychiatrists, American Association for Geriatric Psychiatry, American Association of Chairs of Departments of Psychiatry, American Association of Directors of Psychiatric Residency Training, American Board of Psychiatry and Neurology, American College of Neuropsychopharmacology, American Academy of Pediatrics, American Academy of Family Physicians, American Academy of Physicians, American Academy of Physician Assistants, American Academy of Nurse Practitioners |
| Authorized representatives for inpatient and outpatient pharmacies certified in the Clozapine REMS | REMS Letter: Pharmacy Letter with attachment Factsheet: What's Changed with the Clozapine REMS Program for Pharmacies?  
1. Email within 15 calendar days of approval of the REMS modification and again 15 calendar days later.  
   a. Send by mail or fax within 7 calendar days of the date the second email was sent if email was reported undeliverable or unopened.                                                                                       |
| Inpatient and outpatient pharmacies likely to dispense clozapine               | REMS Letter: Pharmacy Professional Society Letter with attachments Factsheet: What's Changed with the Clozapine REMS Program for Pharmacies?, Drop In Summary for Pharmacies  
1. Disseminate, within 15 calendar days of the approval of the REMS modification, through the following professional societies and request the letter or content be provided to their members:  
   a. American Pharmacists Association, American Society of Health System Pharmacists, National Association of Chain Drug Stores, American College of Clinical Pharmacy, College of Psychiatric and Neurologic Pharmacists, National Community Pharmacists Association, National Association of Specialty Pharmacies, Pharmaceutical Care Management Association |
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<thead>
<tr>
<th>Target Audience</th>
<th>Communication Materials &amp; Dissemination Plans</th>
</tr>
</thead>
</table>
| Wholesalers-distributors enrolled in the Clozapine REMS | REMS Letter: Wholesaler-Distributor Letter with attachment Factsheet: What’s Changed with the Clozapine REMS Program for Pharmacies?  
1. Email within 30 calendar days of approval of the REMS modification and again 15 calendar days later.  
a. Send by mail or fax within 7 calendar days of the date the second email was sent if email was reported undeliverable or unopened.  
2. Request the Factsheet be provided one time to all pharmacies ordering clozapine between August 21, 2021 and December 31, 2021. |
| Healthcare providers                               | Website Pop-Up Message 1  
1. Publish prominently on www.clozapinerems.com within 7 calendar days of the approval of the REMS modification and display for 109 calendar days. The Message must appear the first time a stakeholder logs into the system following launch of the message and require an active click to close it.  
Important Program Update  
1. Publish prominently at www.clozapinerems.com within 7 calendar days of the approval of the REMS modification and display for 109 calendar days.  
Website Pop-Up Message 2  
1. Publish prominently on the public homepage at www.clozapinerems.com on November 15, 2021 and display for 90 calendar days. The Message must appear with each visit to the homepage and require an active click to close it. |

**To support REMS program operations, Clozapine Applicants must:**

1. Authorize dispensing for each patient based on verifying the patient is enrolled, and receipt of the Patient Status Form on the following schedule:  
   Authorize the first dispensing based on receipt of the Patient Enrollment Form.  
   For subsequent dispensings, the Patient Status Form must be received within 37 calendar days after the date of the last Patient Status Form. If the Patient Status Form is not received within 37 calendar days, the patient is not authorized to receive the drug until a completed form is received or a current ANC (result obtained within the last 30 calendar days) within the acceptable range is provided to a pharmacist up to three times per patient per year for outpatient dispensings.

2. Establish and maintain the REMS program website, www.clozapinerems.com. The REMS program website must include the capability to: complete prescriber and pharmacy certification online, enroll and manage patients online including ANC results and patient authorization status; and print the Prescribing Information, Medication Guide, and REMS materials. All product websites for healthcare providers and consumers must include prominent REMS-specific links to the REMS program website. The REMS program website must not link back to the promotional product websites.

3. Make the REMS Program website fully operational and all REMS materials available through the website and coordinating center within 117 calendar days of the REMS modification (November 15, 2021).

4. Establish and maintain a REMS Program coordinating center for REMS participants at 888-586-0758.

5. Establish and maintain a validated, secure database of all REMS participants who are enrolled and/or certified in the Clozapine REMS Program.
6. Ensure that prescribers and pharmacies are able to become certified by fax and online.

7. Ensure prescribers are able to enroll patients by fax and online.

8. Ensure prescribers are able to report ANC results by phone, fax using the Patient Status Form, and online.

9. Ensure pharmacies are able to report ANC results by phone, fax using the ANC Lab Reporting Form and online.

10. Ensure prescribers are able to authorize continuing clozapine treatment for patients when the prescriber determines the benefits outweigh the risks of developing severe neutropenia by fax, phone, and online.

11. Ensure pharmacies are able to enroll as inpatient (for purposes of this REMS, including but not limited to a pharmacy dispensing clozapine only to patients receiving inpatient medical care and other related services for surgery, acute medical conditions, or injuries (usually for a short-term illness or condition)) or outpatient (for purposes of this REMS, including but not limited to retail drug stores, ambulatory care pharmacies, and pharmacies dispensing to long-term care, rehabilitation facilities, and prison systems).

12. Ensure pharmacies are able to obtain authorization to dispense by phone and online.

13. Provide Clozapine and the Risk of Neutropenia: A Guide for Healthcare Providers to Healthcare Providers who (1) Attempt to prescribe clozapine and are not yet certified, or (2) Inquire about how to become certified.

14. Provide Clozapine and the Risk of Neutropenia: A Guide for Pharmacists to pharmacists who (1) Attempt to dispense clozapine and are not yet certified, or (2) Inquire about how to become certified.

15. Notify prescribers and pharmacies within 24 hours after they become certified in the REMS program.

16. Provide certified prescribers access to the database of certified pharmacies and enrolled patients.

17. Provide certified pharmacies access to the database of certified prescribers and enrolled patients.

18. Provide authorized wholesalers-distributors access to the database of certified pharmacies.

19. Establish and maintain a registry which includes a reporting and collection system for all patients to provide information on severe neutropenia.

20. Ensure that once a report of severe neutropenia resulting in hospitalization or death is received, Clozapine Applicants follow up with the healthcare provider to obtain all required data for the registry.

**To ensure REMS participants’ compliance with the REMS program, Clozapine Applicants must:**

21. Ensure the Patient Status Form is received for each patient enrolled in the REMS Program: If the form is not received within 31 calendar days of the date of the last Patient Status Form, Clozapine Applicants must contact the prescriber for the form.

22. Maintain adequate records to demonstrate that the REMS requirements have been met, including, but limited to records of: clozapine distribution and dispensing; certification of prescribers, and pharmacies, and authorization of wholesalers-distributors; enrolled patients; and audits of REMS participants. These records must be readily available for FDA inspections.

23. Establish a plan for addressing noncompliance with REMS Program requirements.
24. Monitor prescribers, pharmacies, and wholesalers-distributors on an ongoing basis to ensure the requirements of the Clozapine REMS Program are being met. Take corrective action if noncompliance is identified, including de-certification.

25. Verify every two years that the designated authorized representative for the pharmacy is the same. If different, the pharmacy must re-certify with a new authorized representative.

26. Audit annually 10% of certified outpatient pharmacies (maximum 400) and 10% of certified inpatient pharmacies (maximum 400) that have ordered clozapine in the previous 12 months to ensure that all processes and procedures are in place, functioning, and support the REMS Program requirements.

27. Audit wholesaler-distributors no later than 180 calendar days after the wholesaler-distributor is authorized and annually thereafter to ensure that all processes and procedures are in place, functioning, and support the REMS Program requirements. The annual audit must include all wholesalers-distributors that distributed clozapine in the previous 12 months.

28. Take reasonable steps to improve implementation of and compliance with the requirements of the Clozapine REMS Program based on monitoring and evaluation of the Clozapine REMS Program.

**IV. REMS Assessment Timetable**

Clozapine NDA Applicants must submit REMS Assessments 18 months from the date of the approval of the July 21, 2021 modification and every 18 months thereafter. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 calendar days before the submission date for that assessment. Clozapine NDA Applicants must submit each assessment so that it will be received by the FDA on or before the due date.

**V. REMS Materials**

The following materials are part of the Clozapine REMS:

**Enrollment Forms**
- Prescriber:
  1. Prescriber Enrollment Form
- Patient:
  2. Patient Enrollment Form
- Pharmacy:
  3. Outpatient Pharmacy Enrollment Form
  4. Inpatient Pharmacy Enrollment Form

**Training and Educational Materials**
- Prescriber:
  6. Knowledge Assessment for Prescribers
- Patient:
  7. A Guide for Patients and Caregivers: What You Need to Know about Clozapine and Neutropenia
- Pharmacy:
  9. Knowledge Assessment for Pharmacists

Reference ID: 4886777
**Patient Care Forms**
10. Patient Status Form
11. ANC Lab Reporting Form

**Communication Materials**
12. Healthcare Provider Letter
14. Drop In Summary for Healthcare Providers
15. Pharmacy Letter
16. Pharmacy Professional Society Letter
17. Drop In Summary for Pharmacies
18. Wholesaler-Distributor Letter
19. Factsheet: What's Changed with the Clozapine REMS Program for Prescribers
20. Factsheet: What’s Changed with the Clozapine REMS Program for Pharmacies
21. Website Pop-Up Message 1
22. Website Pop-Up Message 2
23. Important Program Update

**Other Materials**
24. REMS program website (www.ClozapineREMS.com)
Prescribers who prescribe clozapine only to patients receiving inpatient medical care and other related services for surgery, acute medical conditions or injuries (usually for a short-term illness or condition) are not required to be certified in the Clozapine REMS. Patients in this setting are required to be enrolled in the Clozapine REMS in order to receive clozapine.

For immediate certification, please go to www.clozapinerems.com.

Instructions

Clozapine is only available through the Clozapine REMS (Risk Evaluation and Mitigation Strategy). In order to become certified and prescribe clozapine, you must:
2. Successfully complete and submit the Clozapine REMS Knowledge Assessment for Prescribers
3. Complete and submit this one-time Clozapine REMS Prescriber Enrollment Form

Prescriber Responsibilities

I have:
• Reviewed the drug’s Prescribing Information for clozapine.
• Successfully completed the Knowledge Assessment for Prescribers and submitted it to the Clozapine REMS.

Before treatment initiation (first dose), I must:
• Counsel the patient or caregiver on the risks associated with clozapine, including severe neutropenia, and the Clozapine REMS requirements including to report signs of infection using A Guide for Patients and Caregivers: What You Need to Know about Clozapine and Neutropenia.
• Provide a copy of the Guide to the patient unless clinical judgment indicates that the patient’s adherence to the treatment regimen will be negatively impacted by providing the Guide.
• Assess the patient’s absolute neutrophil count (ANC). Document and submit the ANC to the Clozapine REMS using the Patient Enrollment Form.
• Enroll the patient in the Clozapine REMS by completing and submitting the Patient Enrollment Form to the Clozapine REMS.

During treatment; according to the monitoring frequency in the Prescribing Information, I must
• Assess the patient’s ANC and monitoring frequency.
• For patients with an ANC that falls below the acceptable range: Assess the patient’s health status for appropriateness of continuing treatment.

During treatment, monthly, I must:
• Document and submit the ANC results, the monitoring frequency, and appropriateness for continuing treatment to the Clozapine REMS using the Patient Status Form.

After treatment discontinuation; according to the monitoring frequency in the Prescribing Information, I must:
• Assess the patient’s ANC. Document and submit the ANC results to the REMS program using the Patient Status Form.

I understand that if I do not maintain compliance with the requirements of the Clozapine REMS, I will no longer be able to prescribe Clozapine.

I understand that personnel from the Clozapine REMS or a designated third party acting on behalf of the Clozapine Sponsors may contact me to gather information, resolve discrepancies, or to provide other information related to the Clozapine REMS.

I understand that clozapine manufacturers or their agents and contractors may contact me via phone, mail or email to survey me on the effectiveness of the program requirements for the Clozapine REMS.

Continued on the next page

For more information or materials, contact the Clozapine REMS at www.clozapinerems.com or 1-888-586-0758.

Reference ID: 4886777
# Prescriber Information (All Fields Required Unless Otherwise Indicated)

<table>
<thead>
<tr>
<th>Field</th>
<th>Input Details</th>
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<tbody>
<tr>
<td>First Name</td>
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<td>MI (opt):</td>
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<tr>
<td>Last Name</td>
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<tr>
<td>Individual NPI #</td>
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<tr>
<td>Individual DEA #</td>
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<tr>
<td>Email Address</td>
<td></td>
</tr>
<tr>
<td>Credentials</td>
<td>☐ MD ☐ NP ☐ PA ☐ DO ☐ Other</td>
</tr>
<tr>
<td>Clinic/Practice Name</td>
<td></td>
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<tr>
<td>Address</td>
<td></td>
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<tr>
<td>City</td>
<td></td>
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<td>State</td>
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<td>Zip Code</td>
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<td>Phone</td>
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<td>Ext (opt):</td>
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<td>Fax (opt):</td>
<td></td>
</tr>
<tr>
<td>Preferred Time of Contact</td>
<td>☐ Morning ☐ Afternoon ☐ Evening</td>
</tr>
<tr>
<td>Preferred Method of Contact</td>
<td>☐ Text to Mobile # ☐ Email ☐ Phone Call</td>
</tr>
<tr>
<td>Prescriber’s Signature</td>
<td></td>
</tr>
<tr>
<td>Date (MM/DD/YYYY):</td>
<td></td>
</tr>
</tbody>
</table>

Submit this form:
- Online at [www.clozapinerems.com](http://www.clozapinerems.com)
- Via fax to 1-800-878-5927

You will receive a confirmation via email.
Patient Enrollment Form

Instructions for Prescribers and Prescriber Designees

This form may be completed by a certified prescriber or a prescriber designee.

Complete this form for a patient if:
- re-enrolling a patient into the Clozapine REMS
- the patient has never been treated with clozapine previously, or
- you have never treated this patient with clozapine (regardless of the patient’s history of clozapine treatment)

A prescriber must complete the form to designate the patient as a Benign Ethnic Neutropenia (BEN) patient or a Hospice Care patient. A prescriber designee may not complete the form for these patients.

For immediate enrollment, please go to www.clozapinerems.com.

For enrollment via fax, please complete all required fields below and fax to 800-878-5927. For enrollment via the Clozapine REMS Contact Center, please call 888-586-0758. Enrollment confirmation will be sent via the contact preference specified on the prescriber’s Clozapine REMS Prescriber Enrollment Form.

Clozapine is only available through the single shared Clozapine REMS (Risk Evaluation and Mitigation Strategy). In order to treat a patient with clozapine, the patient MUST be enrolled in the Clozapine REMS. To enroll a patient, you must:

1. Inform the patient or caregiver about the risk of severe neutropenia with clozapine and the Clozapine REMS requirements including to report signs of infection
2. Provide the patient or caregiver with A Guide for Patients and Caregivers: What You Need to Know about Clozapine and Neutropenia unless you determine that the patient’s adherence to the treatment regimen will be negatively impacted by providing the A Guide for Patients and Caregivers: What You Need to Know about Clozapine and Neutropenia and informing them about this risk
3. Complete and submit this Clozapine REMS Patient Enrollment Form

Patient Information (* Required Field)

First Name*: [Input]

Last Name*: [Input]

Gender*:  
- ☐ Male  
- ☐ Female  
- ☐ Other

Date of Birth* (MM/DD/YYYY): / / 

Race*:  
- ☐ American Indian or Alaska Native  
- ☐ Asian  
- ☐ Black or African American  
- ☐ Caucasian  
- ☐ Native Hawaiian or Other Pacific Islander  
- ☐ Other: ________________________________

Ethnicity*:  
- ☐ Hispanic or Latino  
- ☐ Not Hispanic or Latino

Phone: [Input]  

Email Address: [Input]

Does the patient have a permanent address*?  
- ☐ Yes  
- ☐ No  

Zip Code: [Input]

Patient Status (* Required Field)

Is this patient actively on clozapine therapy*?  
- ☐ Yes  
- ☐ No  
- ☐ Unknown

If Yes, what is this patient’s current monitoring frequency?  
- ☐ 3 times a week  
- ☐ Every 2 weeks  
- ☐ Weekly  
- ☐ Monthly

Baseline or Most Recent Lab Information (All Fields Required)

Blood Draw Date (MM/DD/YYYY): [Input]  

ANC (per µL): [Input]

Continued on next page

07/2021

For more information or materials, contact the Clozapine REMS at www.clozapinerems.com or 1-888-586-0758.
## Prescriber Information (* Required Field)

<table>
<thead>
<tr>
<th>First Name*</th>
<th>Last Name*</th>
<th>Individual NPI Number*</th>
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## Prescriber Designee Information (All Fields Required if Form is Completed by a Prescriber Designee)

<table>
<thead>
<tr>
<th>First Name*</th>
<th>Last Name*</th>
<th>Email:</th>
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<table>
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<tr>
<th>Phone*</th>
<th>Fax:</th>
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</table>

## Benign Ethnic Neutropenia (BEN) Patient Attestation (Prescriber signature required for attestation of BEN diagnosis)

A BEN patient designation provides a separate ANC monitoring algorithm for the patient. The BEN designation is a permanent status. By signing below, I attest that the above is a patient with documented benign ethnic neutropenia.

Prescriber Signature: ___________________________  Date (MM/DD/YYYY): ___________________________

## Hospice Care Patient Attestation (Prescriber signature required for attestation of Hospice Care)

For hospice patients (i.e., terminally ill patients with an estimated life expectancy of six months or less), the prescriber may reduce the frequency of submitting a Patient Status Form to once every 6 months after a discussion with the patient and his/her caregiver. To change the frequency of submitting a Patient Status Form to once every 6 months for a hospice patient, the prescriber must sign below:

By signing below, I attest that the above is a hospice care patient.

Prescriber Signature: ___________________________  Date (MM/DD/YYYY): ___________________________
Outpatient Pharmacy Enrollment Form

Complete this form if your pharmacy dispenses clozapine only to patients treated on an outpatient or chronic basis, including, but not limited to, retail drug stores, ambulatory care pharmacies, and pharmacies dispensing to long-term care, rehabilitation facilities, and prison systems.

For immediate certification, please go to www.clozapinerems.com.

Instructions

Use this form to enroll a SINGLE pharmacy location. To enroll MULTIPLE pharmacy locations, you must go to www.clozapinerems.com.

Clozapine is only available through the Clozapine REMS (Risk Evaluation and Mitigation Strategy). In order to dispense clozapine, the pharmacy must designate an authorized representative.

The authorized representative for the pharmacy must:
2. Successfully complete and submit the Knowledge Assessment for Pharmacies.
3. Complete and submit this Outpatient Pharmacy Enrollment.

Authorized Representative Responsibilities

As the Authorized Representative, I must:

- Successfully complete the Knowledge Assessment for Pharmacies and submit it to the Clozapine REMS.
- Establish processes and procedures to verify an available, current ANC is within the acceptable range for patients enrolled but not authorized to receive the drug.
- Train all relevant staff involved in dispensing clozapine on the requirements of the Clozapine REMS using the Clozapine and the Risk of Neutropenia: A Guide for Pharmacists.

Before dispensing, all pharmacy staff must:

- Obtain authorization to dispense each prescription by contacting the Clozapine REMS to verify that the patient is enrolled and authorized to receive drug.
- For patients enrolled but not authorized to receive clozapine:
  - Verify an available, current ANC is within the acceptable range through the processes and procedures established as a requirement of the Clozapine REMS,
  - Document and submit the ANC and the prescriber’s NPI to the Clozapine REMS and
  - Obtain authorization to dispense each prescription by contacting the Clozapine REMS to verify the patient is now authorized to receive clozapine.
- Report dosing information to the Clozapine REMS.

All pharmacy staff must:

- Not distribute, transfer, loan, or sell clozapine except to certified dispensers.
- Maintain records of staff training and that all processes and procedures are in place and are being followed.
- Comply with audits carried out by the manufacturers or a third party acting on behalf of the manufacturers, to ensure that all processes and procedures are in place and are being followed.

To maintain certification to dispense, any new Authorized Representative must:

- Enroll in the Clozapine REMS by reviewing Clozapine and the Risk of Neutropenia: A Guide for Pharmacists, successfully complete the Knowledge Assessment for Pharmacies and the Outpatient Pharmacy Enrollment Form and submit both to the Clozapine REMS.

Continued on Page 2
### Outpatient Pharmacy Information (All Fields Required Unless Otherwise Indicated)

<table>
<thead>
<tr>
<th>Pharmacy Name:</th>
<th>Organization NPI #:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Address:</td>
<td>DEA # (opt.)</td>
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<tr>
<td>City:</td>
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<td>Zip Code:</td>
</tr>
<tr>
<td>Phone:</td>
<td>Ext (opt):</td>
</tr>
<tr>
<td></td>
<td>Fax (opt.):</td>
</tr>
</tbody>
</table>

The name, location, and phone number of your pharmacy will be publicly available on ClozapineREMS.com. If you do not want your information available, please call the Clozapine REMS Contact Center at 1-888-586-0758.

Allow this pharmacy to be found on the Clozapine REMS website as:  
- [ ] Retail Pharmacy  
- [ ] Specialty Pharmacy

### Authorized Representative Information (All Fields Required Unless Otherwise Indicated)

<table>
<thead>
<tr>
<th>First Name:</th>
<th>Last Name:</th>
<th>Position/Title:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Email Address:</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Credentials:**  
- [ ] RPh  
- [ ] PharmD  
- [ ] BCPS  
- [ ] Other  
- [ ] Other

<table>
<thead>
<tr>
<th>Phone:</th>
<th>Ext (opt):</th>
<th>Fax (opt.):</th>
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<tbody>
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<td></td>
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</tr>
</tbody>
</table>

**Preferred Method of Contact (opt.):**  
- [ ] Text to Mobile #  
- [ ] Email  
- [ ] Phone Call

**Authorized Representative’s Signature:**

**Date (MM/DD/YYYY):**

Submit this form:  
- Online at [www.clozapinerems.com](http://www.clozapinerems.com)  
- Via fax to 1-800-878-5927

You will receive a confirmation via email.
Inpatient Pharmacy Enrollment Form

Complete this form if your pharmacy is within a facility dispensing clozapine only to patients receiving inpatient medical care and other related services for surgery, acute medical conditions, or injuries (usually for a short-term illness or condition).

If your pharmacy dispenses clozapine only to patients treated on an outpatient or chronic basis, including, but not limited to, retail drug-stores, ambulatory care pharmacies, and pharmacies dispensing to long-term care, rehabilitation facilities, and prison systems, please complete the Clozapine REMS Outpatient Pharmacy Enrollment Form.

For immediate certification, please go to www.clozapinerems.com.

Instructions

Use this form to enroll a SINGLE pharmacy location. To enroll MULTIPLE pharmacy locations, you must go to www.clozapinerems.com.

Clozapine is only available through the Clozapine REMS (Risk Evaluation and Mitigation Strategy). In order to dispense clozapine, the pharmacy must designate an authorized representative.

The authorized representative for the pharmacy must:
2. Successfully complete and submit the Knowledge Assessment for Pharmacies.
3. Complete and submit this Inpatient Pharmacy Enrollment Form.

Authorized Representative Responsibilities

As the Authorized Representative, I must:
• Successfully complete the Knowledge Assessment for Pharmacies and submit it to the Clozapine REMS.
• Establish processes and procedures to verify an available, current ANC is within the acceptable range for patients enrolled but not authorized to receive clozapine.
• Train all relevant staff involved in dispensing clozapine on the requirements of the Clozapine REMS, using the Clozapine and the Risk of Neutropenia: A Guide for Pharmacists.

Before first dose, all pharmacy staff must:
• Obtain authorization to dispense by contacting the Clozapine REMS to verify that the patient is enrolled and authorized to receive the drug.
• For patients enrolled but not authorized to receive clozapine:
  o Verify an available, current ANC is within the acceptable range through the processes and procedures established as a requirement of the Clozapine REMS,
  o Document and submit the ANC to the Clozapine REMS and
  o Obtain authorization to dispense each prescription by contacting the Clozapine REMS to verify the patient is now authorized to receive clozapine.

At discharge, all pharmacy staff must:
• Dispense no more than a 7-days’ supply.

At all times, all pharmacy staff must:
• Maintain records of staff training and that all processes and procedures are in place and are being followed.
• Not distribute, transfer, loan, or sell clozapine except to certified dispensers.
• Comply with audits carried out by the manufacturers or a third party acting on behalf of the manufacturers, to ensure that all processes and procedures are in place and are being followed.

To maintain certification to dispense, any new Authorized Representative must:
• Enroll in the Clozapine REMS by reviewing Clozapine and the Risk of Neutropenia: A Guide for Pharmacists, successfully complete the Knowledge Assessment for Pharmacies and the Inpatient Pharmacy Enrollment Form and submit both to the Clozapine REMS.

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For more information or materials, contact the Clozapine REMS at www.clozapinerems.com or 1-888-566-0758.

Reference ID: 4886777
# Inpatient Pharmacy Enrollment Form

## Inpatient Pharmacy Information (All Fields Required Unless Otherwise Indicated)

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<th>Pharmacy Name:</th>
<th>Organization NPI #:</th>
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<tbody>
<tr>
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<td>DEA # (opt.)</td>
</tr>
<tr>
<td>City:</td>
<td>State:</td>
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<td></td>
<td>Zip Code:</td>
</tr>
<tr>
<td>Phone:</td>
<td>Ext (opt):</td>
</tr>
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<td></td>
<td>Fax (opt.):</td>
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## Authorized Representative Information (All Fields Required Unless Otherwise Indicated)

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<th>First Name:</th>
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<th>Position/Title:</th>
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</thead>
<tbody>
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<td>Email Address:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Credentials: □ RPh □ PharmD □ BCPS □ Other</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phone:</td>
<td>Ext (opt):</td>
<td>Fax (opt.):</td>
</tr>
<tr>
<td>Preferred Method of Contact (opt.): □ Text to Mobile # □ Email □ Phone Call</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Authorized Representative’s Signature:** ____________________________  **Date (MM/DD/YYYY):** __________

---

**Submit this form:**
- Online at [www.clozapinerems.com](http://www.clozapinerems.com)
- Via fax to 1-800-878-5927

*You will receive a confirmation via email*
Clozapine and the Risk of Neutropenia:
A Guide for Healthcare Providers

This Guide discusses:
- What is the Clozapine REMS?
- Clozapine and the risk of severe neutropenia
- Treatment recommendations and patient absolute neutrophil count (ANC) monitoring
- Prescriber requirements for the Clozapine REMS
- Pharmacy requirements for the Clozapine REMS

Look for this symbol to point out changes to the Clozapine REMS.
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### The Clozapine REMS

Clozapine is associated with severe neutropenia (absolute neutrophil count (ANC) less than 500/µL). The requirements to prescribe, dispense, and receive clozapine are incorporated into a single shared program called the Clozapine Risk Evaluation and Mitigation Strategy (REMS). A REMS is a strategy to manage known or potential risks associated with a drug or group of drugs and is required by the Food and Drug Administration (FDA) for clozapine to ensure that the benefits of the drug outweigh the risk of severe neutropenia.

The Clozapine REMS provides a **centralized** point of access:
1. For **prescribers** and **pharmacies** to certify before prescribing or dispensing clozapine
2. To enroll and manage **patients** on clozapine treatment

Clozapine is available by prescription as:
- Clozaril® (clozapine) tablets, for oral use
- Versacloz® (clozapine, USP) oral suspension
- Approved generic equivalents of these products

To **minimize the risk of severe neutropenia associated with the use of clozapine**, the Clozapine REMS includes the following key program requirements:

#### Prescribers (who prescribe clozapine for outpatient use or initiate treatment for inpatients)
- Must certify in the Clozapine REMS to prescribe clozapine
- Must enroll all patients in the Clozapine REMS
- Must provide a baseline ANC when enrolling a new patient
- Must order ANC testing for each of their clozapine patients according to the clozapine Prescribing Information
- Must verify and document each clozapine patient’s ANCs to the Clozapine REMS monthly, by submitting the Patient Status Form

#### Outpatient Pharmacies
- Must certify in the Clozapine REMS to dispense clozapine
  - Must obtain a REMS Dispense Authorization (RDA) prior to dispensing a clozapine prescription. For the first dispensing after enrollment, the RDA will verify that:
    - the pharmacy is certified
    - the patient is enrolled
    - the patient’s treatment is not interrupted or discontinued
  - For a subsequent dispensing, the RDA will verify that:
    - the pharmacy is certified
    - the patient is enrolled
    - a Patient Status Form has been completed in the last 37 days
      - the prescriber has authorized the continuation of treatment if one or more labs are missing
      - the prescriber has provided a Treatment Rationale if the most current ANC lab value is below the acceptable range
    - the patient’s treatment is not interrupted or discontinued

#### Inpatient Pharmacies
- Must certify in the Clozapine REMS to dispense clozapine
  - Must obtain a REMS Dispense Authorization (RDA) before the **initial** dispensing of a clozapine prescription. For the first dispensing after enrollment, the RDA will verify that:
    - the pharmacy is certified
Clozapine and the Risk of Neutropenia:
A Guide for Prescribers

- the patient is enrolled
- the patient's treatment is not interrupted or discontinued

For a subsequent dispensing, the RDA will verify that:
- the pharmacy is certified
- the patient is enrolled
- a Patient Status Form has been completed in the last 37 days
  - the prescriber has authorized the continuation of treatment if one or more labs are missing
  - the prescriber has authorized a Treatment Rationale if the most current ANC lab value is below the acceptable range
- the patient's treatment is not interrupted or discontinued

**Patients**
- Must be enrolled in the Clozapine REMS by a certified prescriber to receive clozapine
- Must comply with the ANC testing requirements
2 Absolute Neutrophil Count (ANC), Neutropenia, and Patient ANC Monitoring

What is Absolute Neutrophil Count (ANC)?

ANC is the laboratory parameter for monitoring patients for clozapine-induced neutropenia. Prescribers must submit the ANC before starting and during clozapine treatment.

ANC is usually available as a component of the complete blood count (CBC), including differential:

- ANC is more relevant to drug-induced neutropenia than white blood cell (WBC) count
- ANC may also be calculated using the following formula:

\[
\text{Absolute Neutrophil Count} = \frac{\text{Total WBC Count}}{\text{Total percentage of neutrophils* obtained from the differential}}
\]

*Includes both banded and segmented neutrophils

Other granulocytes (basophils and eosinophils) contribute minimally to neutropenia and their measurement is not necessary.

What is the risk of severe neutropenia associated with clozapine?

Clozapine can cause severe neutropenia, which can lead to serious infections and death. Severe neutropenia occurs in a small percentage of patients taking clozapine.

- Severe neutropenia is defined as ANC less than 500/µL
- “Severe neutropenia” replaces the previous terms “severe leukopenia,” “severe granulocytopenia,” and “agranulocytosis”
- The risk appears greatest during the first 18 weeks of clozapine treatment
- The mechanism is not dose-dependent
- It is unclear if concurrent use of other drugs known to cause neutropenia increases the risk or severity of clozapine-induced neutropenia
- If clozapine is used concurrently with a medication(s) known to cause neutropenia:
  - Consider monitoring patients more closely than the treatment guidelines recommend, and
  - Consult with the treating oncologist in patients receiving concomitant chemotherapy

For a complete discussion of other risks, including other Boxed Warnings, please see the full Prescribing Information available at www.clozapinerems.com.
What is Benign Ethnic Neutropenia (BEN)?

BEN is a condition observed in certain ethnic groups whose average ANCs are lower than “standard” laboratory ranges for neutrophils. Because of this condition, patients who have been diagnosed with BEN have a separate ANC monitoring algorithm when treated with clozapine.

When enrolling a patient in the Clozapine REMS, identify if the patient has documented BEN, so the patient is monitored according to the correct ANC monitoring algorithm.

A few important things to know about patients with documented BEN:
- It is most commonly observed in individuals of African descent (approximate prevalence of 25-50%), 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. Consider a hematology consultation before starting or during clozapine treatment as necessary.

What are the treatment recommendations and monitoring requirements for patients taking clozapine?

Before starting treatment with clozapine, the baseline ANC must be:
- at least 1500/µL for the general population
- at least 1000/µL for patients diagnosed with BEN

During treatment, monitor ANC regularly as described in Table 1 and Table 2 below.

Patients may transition to less frequent ANC monitoring based on the number of weeks of continuous clozapine therapy and the patient’s ANCs.

During the first six months of treatment:
- Weekly ANC monitoring is required for all patients

During the second six months of treatment:
- Monitoring frequency can be reduced to every two weeks if the ANC remains in the normal range (ANC greater than or equal to 1500/µL for the general population, ANC greater than or equal to 1000/µL for patients with BEN)

After one year of treatment:
- If the patient’s ANC continues to remain in the normal range, ANC monitoring may be reduced to monthly (every 4 weeks) thereafter.
The recommended ANC monitoring frequency for patients in the general population and patients who have documented BEN is shown in Table 1 and Table 2 below. The table also provides recommendations for monitoring patients who experience a decrease in ANC during the course of treatment.

**Table 1 - Recommended Monitoring Frequency and Clinical Decisions by ANC Level for the General Patient Population**

<table>
<thead>
<tr>
<th>ANC Level</th>
<th>Treatment Recommendation</th>
<th>ANC Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Range</td>
<td>• Initiate treatment</td>
<td>• Weekly from initiation to six months</td>
</tr>
<tr>
<td>ANC ≥ 1500/μL</td>
<td>• If treatment interrupted:</td>
<td>• Every two weeks from 6 to 12 months</td>
</tr>
<tr>
<td></td>
<td>- &lt; 30 days, continue monitoring as before</td>
<td>• Monthly after 12 months</td>
</tr>
<tr>
<td></td>
<td>- ≥ 30 days, monitor as if new patient</td>
<td>• See Section 2.4 of the Prescribing Information</td>
</tr>
<tr>
<td></td>
<td>• Discontinuation for reasons other than neutropenia</td>
<td></td>
</tr>
<tr>
<td>Mild Neutropenia</td>
<td>• Continue treatment</td>
<td>• Three times weekly until ANC ≥ 1500/μL</td>
</tr>
<tr>
<td>(1000 - 1499/μL)*</td>
<td></td>
<td>• Once ANC ≥ 1500/μL, return to patient’s last “Normal Range” ANC monitoring interval**</td>
</tr>
<tr>
<td>Moderate Neutropenia</td>
<td>• Recommend hematology consultation</td>
<td>• Daily until ANC ≥ 1000/μL, then:</td>
</tr>
<tr>
<td>(500 - 999/μL)*</td>
<td>• Interrupt treatment for suspected clozapine-induced neutropenia</td>
<td>• Three times weekly until ANC ≥ 1500/μL</td>
</tr>
<tr>
<td></td>
<td>• Resume treatment once ANC normalizes to ≥ 1000/μL</td>
<td>• Once ANC ≥ 1500/μL, check ANC weekly for 4 weeks, then return to patient’s last “Normal Range” ANC monitoring interval**</td>
</tr>
<tr>
<td>Severe Neutropenia</td>
<td>• Recommend hematology consultation</td>
<td>• Daily until ANC ≥ 1000/μL</td>
</tr>
<tr>
<td>(&lt; 500/μL)*</td>
<td>• Interrupt treatment for suspected clozapine-induced neutropenia</td>
<td>• Three times weekly until ANC ≥ 1500/μL</td>
</tr>
<tr>
<td></td>
<td>• Do not rechallenge unless prescriber determines benefits out weigh risks</td>
<td>• If patient rechallenged, resume treatment as a new patient under “Normal Range” monitoring once ANC ≥ 1500/μL</td>
</tr>
</tbody>
</table>

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

** If clinically appropriate
Table 2 Recommended Monitoring Frequency and Clinical Decisions by ANC Level for Patients with BEN

<table>
<thead>
<tr>
<th>ANC Level</th>
<th>Treatment Recommendation</th>
<th>ANC Monitoring</th>
</tr>
</thead>
</table>
| Normal BEN Range  
(Established ANC baseline ≥1000/μL) | - Obtain at least two baseline ANC levels before initiating treatment  
- If treatment interrupted:  
  - < 30 days, continue monitoring as before  
  - ≥ 30 days, monitor as if new patient  
- Discontinuation for reasons other than neutropenia | - Weekly from initiation to 6 months  
- Every 2 weeks from 6 to 12 months  
- Monthly after 12 months  
- See Section 2.4 of the Prescribing Information |
| BEN Neutropenia  
(500 - 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  
(< 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  
- Three times weekly until ANC ≥ patients 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

Can a patient continue clozapine treatment with an ANC less than 1000/μL?

For Patients in the General Population

Yes; prescribers may choose to continue clozapine treatment in patients with ANCs less than 1000/μL. However, prescribers should follow the treatment recommendations as noted in Table 1 and carefully determine if the benefits of continuing clozapine treatment outweigh the risks.

The recommendations to interrupt treatment are provided to ensure patient safety. If monitoring ANC and symptoms of infection is not done appropriately, patients with ANCs less than 1000/μL are at risk for developing complications of severe neutropenia, including serious infection and death.

Refer to Section 3 of this document for more details on how to authorize a patient to continue treatment.

For Patients with documented BEN

Yes; the Prescribing Information for clozapine recommends interrupting clozapine treatment for patients with BEN only when the ANC is less than 500/μL. No interruption in treatment is recommended for ANC 500-999/μL, although a hematology consultation is recommended.

Reference ID: 4886777
If a patient develops a fever, how is clozapine treatment managed?

Generally, clozapine treatment should be interrupted as a precautionary measure in any patient who develops a fever of 38.5°C (101.3°F) or greater, and an ANC should be obtained. Fever is often the first sign of a neutropenic infection.

If fever occurs in any patient with an ANC less than 1000/µL, initiate appropriate neutropenia work-up and treatment for infection. Refer to Table 1 for ANC monitoring recommendations.

If any patient presents with evidence of fever and/or neutropenia, consider a hematology consultation.

How is clozapine discontinued for neutropenia?

The method of treatment discontinuation will vary depending on the patient’s most recent ANC result. Abrupt treatment discontinuation is necessary for moderate to severe neutropenia that you suspect is caused by clozapine.

REMEMBER to submit the decision to discontinue clozapine for a patient to the Clozapine REMS. You can complete this in one of three ways:

- By signing in to the Clozapine REMS Website at www.clozapinerems.com
- By calling the Clozapine REMS Contact Center at 888-586-0758
- By completing the “Patient Status” section of the Clozapine REMS Patient Status Form and faxing it to the Clozapine REMS at 800-878-5927

How is a patient monitored if clozapine treatment is discontinued for neutropenia?

- Monitor ANC in any patient reporting a fever (temperature of 38.5°C or 101.3°F or greater) during the 2 weeks after discontinuation
- Monitor all patients carefully for the recurrence of psychotic symptoms and symptoms related to cholinergic rebound, such as profuse sweating, headache, nausea, vomiting, and diarrhea
- For abrupt clozapine discontinuation for a reason unrelated to neutropenia, continuation of the existing ANC monitoring is recommended for general population patients until their ANC is greater than or equal to 1500/µL and for patients with documented BEN until their ANC is greater than or equal to 1000/µL or above their baseline

After discontinuing clozapine, monitor ANC according to the recommendations in Table 2 as shown below.
Table 2: Recommended monitoring frequency when clozapine treatment is discontinued

<table>
<thead>
<tr>
<th>Neutropenia</th>
<th>GENERAL POPULATION</th>
<th>BEN POPULATION</th>
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</thead>
<tbody>
<tr>
<td>Moderate Neutropenia (500 to 999/µL)*</td>
<td>• Daily until ANC ≥ 1000/µL, then&lt;br&gt;• Three times weekly until ANC ≥ 1500/µL</td>
<td>• Daily until ANC ≥ 500/µL&lt;br&gt;• Three times weekly until ANC ≥ patients established baseline</td>
</tr>
<tr>
<td>Severe Neutropenia (less than 500/µL)*</td>
<td>• Daily until ANC ≥ 1000/µL, then&lt;br&gt;• Three times weekly until ANC ≥ 1500/µL</td>
<td></td>
</tr>
</tbody>
</table>

* Confirm all initial reports of ANC less than 1500/µL (ANC < 1000/µL for BEN patients) with a repeat ANC measurement within 24 hours

Refer to Section 2.4 of the clozapine Prescribing Information for further information.

Can a patient be rechallenged with clozapine?

Yes; for some patients who experience, or have experienced, moderate clozapine-related neutropenia (ANC less than 1000/µL) or severe clozapine-related neutropenia (ANC less than 500/µL), the risk of serious psychiatric illness from discontinuing clozapine may be greater than the risk of rechallenge. This may be relevant for patients with severe schizophrenic illness who have no treatment option other than clozapine.

In making the decision to rechallenge a patient, consider:
- A hematology consult
- The ANC ranges defined in the Prescribing Information
- The patient’s medical and psychiatric history
- A discussion with the patient and his or her caregiver about the benefits and risks of clozapine rechallenge
- The severity and characteristics of the neutropenic episode

Refer to Section 2.5 in the clozapine Prescribing Information for more information on how to restart clozapine in patients who have discontinued clozapine.
**What is the role of prescribers in the Clozapine REMS?**

**Step 1:** Review the Prescribing Information for clozapine

**Step 2:** Certify* in the Clozapine REMS by:
- Reviewing *Clozapine and the Risk of Neutropenia: A Guide for Prescribers*
- Successfully complete and submit the *Knowledge Assessment for Prescribers*
- Complete and submit the *Prescriber Enrollment Form*

**Step 3:** Counsel each patient (or their caregiver) about the risk of severe neutropenia, which can lead to serious infection and death

**Step 4:** Enroll every new patient in the Clozapine REMS, providing an ANC with the enrollment

**Step 5:** Check the ANC for each patient according to the monitoring requirements

**Step 6:** Submit each patient’s ANCs to the Clozapine REMS monthly, using the *Patient Status Form*

**Step 7:** Provide authorization to continue treatment, if necessary, through the Clozapine REMS when the patient’s ANC results meet criteria for interruption of therapy, and you decide to continue clozapine treatment

Refer to the section titled, “What is a Treatment Rationale?” on page 14 for more details on how to authorize a patient to continue treatment.

*Prescribers who prescribe clozapine only to patients receiving inpatient medical care and other related services for surgery, acute medical conditions or injuries (usually for a short-term illness or condition) are not required to certify in the Clozapine REMS. Patients in this setting are required to be enrolled in the Clozapine REMS in order to receive clozapine. If a patient in this setting is not enrolled, he/she must be enrolled by a certified prescriber before being allowed to receive clozapine.
**How do I Designate a Prescriber Designee?**

Prescribers may designate other healthcare providers or office staff to enroll patients and submit ANC results monthly, using the Patient Status Form, on the prescriber’s behalf.

Visit [www.clozapinerems.com](http://www.clozapinerems.com).

To enroll a prescriber designee online, log into your account and select the Manage Designees button. Select the Invite Designee button. Follow the instructions. The designee will receive an email with a link to allow them to create an account. Once created, the designee may log into their account and enroll patients and submit ANC results monthly, using the Patient Status Form, on your behalf.

To enroll a prescriber designee via fax, print out the Prescriber Designee Enrollment Form. Complete all sections. Both you and the designee must sign the form. Fax the form to 800-878-5927.

**What do I tell my patients about clozapine?**

- Tell your patients about the risk of severe neutropenia which can lead to serious infections and death.
- Explain the importance of having required blood tests to check if a patient is more likely to get an infection.
- Tell patients to talk to a doctor immediately if they have any symptoms of infection. These symptoms are clearly laid out in the counseling tool. Provide your patient with the counseling tool.

You may choose not to provide *A Guide for Patients and Caregivers: What You Need to Know about Clozapine and Neutropenia* to the patient or caregiver if you determine that the patient’s adherence to clozapine treatment will be negatively impacted by providing it. If you choose to not provide the guide to a patient, remember to talk about the following symptoms:

- Infection, including skin, throat, urinary tract, vaginal, pneumonia, or any other infection
- Pain or burning while urinating
- Fever or chills
- Unusual vaginal discharge or itching
- Sores or ulcers inside your mouth, gums, or on your skin
- Abdominal pain
- Wounds that take a long time to heal
- Sores or pain in or around your rectal area
- Feel like you have the flu
- Feel extremely weak or tired
Clozapine and the Risk of Neutropenia: A Guide for Prescribers

How do I enroll a patient?

You can enroll a patient in one of two ways:

- By signing into the Clozapine REMS Website at www.clozapinerems.com and enrolling the patient online
- By downloading a Patient Enrollment Form from the Clozapine REMS Website at www.clozapinerems.com and faxing the completed form to 800-878-5927

Complete a Clozapine REMS Patient Enrollment Form if:

- The patient has never been treated with clozapine before; or,
- If you have never treated this patient with clozapine, regardless of the patient's history of clozapine treatment

How do I submit ANC results for my patients?

Prescribers and Prescriber Designees

Prescribers or their designees are responsible for submitting ANC monthly, using the Patient Status Form, to the Clozapine REMS before clozapine can be dispensed by an outpatient pharmacy.

For Prescribers in an Outpatient setting:

Submit the Patient Status Form monthly in one of three ways:

- By signing into the Clozapine REMS Website at www.clozapinerems.com
- By calling the Clozapine REMS Contact Center at 888-586-0758
- By faxing* the Patient Status Form results to the Clozapine REMS at 800-878-5927

Pharmacies

Pharmacists must verify that the patient is enrolled in the Clozapine REMS and authorized to receive clozapine before clozapine can be dispensed by a pharmacy within a facility that dispenses clozapine to patients receiving inpatient medical care and other related services for surgery, acute medical conditions, or injuries (usually for a short-term illness or condition).

For patients enrolled but not authorized by the Clozapine REMS to receive clozapine, the pharmacy must verify an available, current ANC is within acceptable range through the processes and procedures established as a requirement of the Clozapine REMS, document and submit the ANC to the Clozapine REMS and obtain authorization to dispense each prescription by contacting the Clozapine REMS to verify the patient is now authorized to receive clozapine. The pharmacy may use either the ANC Reporting Form, the website, or the contact center to report an ANC.

⚠️ While the patient is hospitalized, remember to monitor ANC according to the patient’s ANC monitoring frequency on file with the Clozapine REMS.
When should I submit a patient’s ANC to the Clozapine REMS?

Patient ANC information must be submitted to the Clozapine REMS using the Patient Status Form. Although the Patient Status Form is only submitted monthly, prescribers must ensure their patients are on the appropriate monitoring frequency and adhere to the corresponding blood draw intervals. Single ANCs may still be submitted via the ANC Lab Reporting Form.

Your options to submit ANCs are:
1. Submit all at once via the Patient Status Form monthly
2. Submit as labs are obtained via the ANC Lab Reporting Form

How do I authorize continuation of clozapine when my patient’s ANC is less than 1000/μL (general population) or less than 500/μL (patients with BEN)?

When a patient’s ANC is less than 1000/μL (general population) or less than 500/μL (patients with documented BEN), a prescriber may provide a Treatment Rationale to authorize clozapine treatment to continue.

What is a Treatment Rationale?

An authorization called a Treatment Rationale requires the prescriber to confirm that the benefits of continuing clozapine treatment outweigh the risks of developing severe neutropenia. The Treatment Rationale is a section that is completed on the Patient Status Form.

How can I provide a Treatment Rationale?

- The Clozapine REMS will alert the prescriber if an ANC is submitted that is below the recommended thresholds for a patient; clozapine will not be dispensed to the patient unless the prescriber provides a Treatment Rationale to authorize continuation of treatment.
- The Clozapine REMS will automatically change the treatment status of a patient with a low ANC to “interrupted” or “discontinued,” according to the recommendations in the Prescribing Information, found in Table 1 above.
- If the prescriber wishes to continue clozapine treatment, the prescriber must confirm that the benefits of continuing clozapine treatment outweigh the risks of developing severe neutropenia by providing a Treatment Rationale on the Patient Status Form. The completion of a Treatment Rationale will change the patient’s treatment status back to “active.”

Prescribers must confirm treatment continuation one of two ways:

- By signing into the Clozapine REMS Website at www.clozapinerems.com and submitting a Patient Status Form online
- By faxing a signed Patient Status Form to 800-878-5927 with a completed Treatment Rationale section

• After the prescriber provides the Treatment Rationale, the Clozapine REMS will issue an
RDA, which allows the outpatient pharmacy to dispense clozapine.

- Information provided in the Clozapine REMS is not a substitute for appropriate documentation in the patient’s medical record regarding the prescriber’s decision to continue, interrupt, or discontinue clozapine treatment.

**What if my clozapine patient is under hospice care?**

For hospice patients (i.e., terminally ill patients with an estimated life expectancy of six months or less), the prescriber may reduce the ANC monitoring frequency to, at a minimum, once every six months, after a discussion with the patient and his/her caregiver. Individual treatment decisions should weigh the importance of monitoring ANC in the context of the need to control psychiatric symptoms and the patient’s terminal illness.

Designating a patient as a Hospice Care patient reduces the frequency of submitting a *Patient Status Form* to once every six months.

**What if my patient has been treated with clozapine before?**

If another prescriber has previously treated the patient with clozapine, you must enroll the patient by completing and submitting the *Patient Enrollment Form* to the Clozapine REMS (online or by fax) to be able to access the patient’s ANC history.

If you cannot find the patient, call the Clozapine REMS Contact Center at 888-586-0758 for assistance or to re-enroll the patient.

If you would like to inquire about a patient’s previous clozapine history before enrolling the patient, please call the Clozapine REMS Contact Center at 888-586-0758 for assistance.

**To access patient information through the Clozapine REMS, you must enroll the patient.** If you would like to inquire about a patient’s previous clozapine history before enrolling the patient, please call the Clozapine REMS Contact Center at 888-586-0758 for assistance.
4 Reporting Adverse Events Associated with Clozapine

Report suspected adverse events directly to the Clozapine REMS Contact Center at 888-586-0758. You also may report adverse event information to the FDA MedWatch Reporting System by telephone at (800) FDA-1088 or by mail using Form 3500A, available at www.fda.gov/medwatch.

5 Clozapine REMS Information and Resources

Additional Clozapine REMS information and resources are available online at www.clozapinerems.com or by calling the Clozapine REMS Contact Center at 888-586-0758.

Glossary

**Absolute neutrophil count (ANC):** Laboratory parameter for monitoring patients for clozapine-induced neutropenia.

**Benign Ethnic Neutropenia (BEN):** A condition observed in certain ethnic groups whose average ANC is lower than “standard” laboratory ranges for neutrophils compared to the general population. Patients with documented BEN have a separate ANC monitoring algorithm when treated with clozapine.

**Dispense Rationale:** The Clozapine REMS Program provides certified pharmacies with an opportunity to apply clinical judgment and continue to dispense clozapine to enrolled patients when a Patient Status Form has not been received and the pharmacist is in possession of a current ANC within an acceptable range for the patient.

**Inpatient pharmacy:** A pharmacy within a facility dispensing clozapine only to patients receiving inpatient medical care and other related services for surgery, acute medical conditions or injuries (usually for a short-term illness or condition).

**Outpatient pharmacy:** A pharmacy dispensing clozapine only to patients treated on an outpatient or chronic basis. This includes, but is not limited to, retail drugstores, ambulatory care pharmacies, and pharmacies dispensing to long-term care, rehabilitation facilities and prison systems.
REMS Dispense Authorization (RDA): An authorization given to pharmacies which reflects that the safe-use conditions for that patient have been met. The RDA is provided by the Clozapine REMS. For an outpatient pharmacy, the RDA verifies that the patient is enrolled, the pharmacy is certified, and that the patient is authorized to receive drug. For an inpatient pharmacy, the RDA verifies that the patient is enrolled, and the pharmacy is certified. This RDA permits dispensing of clozapine to the patient.

Treatment Rationale (TR): A justification used by a prescriber to allow a patient having moderate neutropenia (ANC 500-999/µL for the general population) or severe neutropenia (ANC < 500/µL for general population and patients with documented BEN) to continue treatment. Only prescribers can confirm that benefits of continuing clozapine treatment outweigh the risks of developing severe neutropenia.
## Instructions
1. Complete Section 1 below to ensure the Knowledge Assessment is associated with your program record.
2. Answer all questions in Section 2.
3. Fax the completed Knowledge Assessment for Prescribers to the Clozapine REMS at 800-878-5927.

For real-time processing of this Knowledge Assessment, please go to www.clozapinerems.com.

## 1 Prescriber Information (PLEASE TYPE OR PRINT)

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## 2 Knowledge Assessment

Please select the best answer for each of the following questions. All questions must be answered correctly to become certified.

**Question 1**

All clozapine products are only available under the single shared Clozapine REMS.

A. True  
B. False

**Question 2**

Clozapine is associated with severe neutropenia, which can lead to serious infection and death.

A. True  
B. False

**Question 3**

Severe neutropenia is defined as:

A. A white blood cell count (WBC) less than 2000/μL
B. An absolute neutrophil count (ANC) less than 1000/μL
C. An absolute neutrophil count (ANC) less than 500/μL
D. None of the above

**Question 4**

Before initiating treatment with clozapine:

A. A baseline absolute neutrophil count (ANC) must be at least 1000/μL for a patient with documented benign ethnic neutropenia (BEN)
B. A baseline absolute neutrophil count (ANC) must be at least 1500/μL for a patient who is part of the general population (i.e., the patient does not have documented BEN)
C. A baseline absolute neutrophil count (ANC) is not necessary
D. Both A and B

*Continued on next page*
Question 5
Before clozapine treatment initiation, a certified prescriber must:
A. Determine if the patient has documented BEN
B. Enroll the patient in the Clozapine REMS
C. Counsel the patient/caregiver about the risk of severe neutropenia
D. Order blood work to obtain an ANC
E. Review the ANC and submit it to the Clozapine REMS
F. All of the above

Question 6
In the outpatient setting, prescribers must submit the Patient Status Form monthly, to the single shared Clozapine REMS, before the patient can be dispensed clozapine.
A. True
B. False

Question 7
How much clozapine can be dispensed?
A. A 30-day supply
B. A 90-day supply
C. As much as the patient wants or the insurance will pay for
D. It depends when the patient's next blood draw is, according to the monitoring requirements. Dispense enough medication to treat the patient with clozapine until the next blood draw/ANC or as directed by the prescriber

Question 8
Regarding patients with documented BEN, which of the following statements are true?
A. Patients with BEN have a different clozapine treatment algorithm and monitoring requirements
B. Patients with BEN are healthy and do not suffer from repeated severe infections
C. Patients with BEN are NOT at increased risk for developing clozapine-induced neutropenia
D. Before starting clozapine, additional evaluation may be needed to determine if baseline neutropenia is due to BEN. Hematology consultation may be necessary
E. All of the above statements are true

Continued on next page
Question 9
If a new patient’s baseline ANC is within the normal range, how should the ANC monitoring schedule proceed?
A. Weekly from initiation to discontinuation of therapy
B. Weekly from initiation to 6 months; every 2 weeks from 6 to 12 months; monthly after 12 months
C. Monthly from initiation to discontinuation of therapy
D. No additional ANC monitoring is required if the patient’s baseline ANC is within the normal range

Question 10
If a patient’s ANC indicates mild neutropenia, which of the following statements is true?
A. ANC monitoring should be conducted three times weekly until ANC ≥ 1500/μL if the patient is part of the general population (i.e., if the patient does not have documented BEN)
B. Mild neutropenia is within the normal range for a patient with documented BEN
C. If the patient has documented BEN, ANC monitoring should be conducted: weekly from initiation to 6 months; every 2 weeks from 6 to 12 months; monthly after 12 months
D. All of the above

Question 11
If a patient’s ANC indicates moderate neutropenia, which of the following statements is true?
A. Treatment should be continued regardless of whether the patient is part of the general population or has documented BEN
B. If the patient is part of the general population (i.e., if the patient does not have documented BEN), interrupt therapy and conduct ANC monitoring: daily until ANC ≥ 1000/μL; three times weekly until ANC ≥ 1500/μL; weekly for 4 weeks; then return to the patient’s last “Normal Range” ANC monitoring interval
C. The ANC monitoring schedule is the same regardless of whether the patient is part of the general population or has BEN
D. None of the above

Question 12
If a patient’s ANC indicates severe neutropenia, which of the following statements is true?
A. Treatment should be interrupted regardless of whether the patient is part of the general population or has BEN and a hematology consultation should be considered; resume treatment only if the prescriber determines that the benefits of clozapine therapy outweigh the risks
B. If the patient is part of the general population (i.e., if the patient does not have documented BEN), interrupt treatment and conduct ANC monitoring: daily until ANC ≥ 1000/μL; three times weekly until ANC ≥ 1500/μL
C. The patient may still be rechallenged with clozapine at the discretion of the prescriber
D. All of the above

Required for all prescribers
Prescriber Signature: X

Date:

Reference ID: 4886777
Version 1.0 July 2021
A Guide for Patients and Caregivers:

What You Need to Know about Clozapine and Neutropenia

Patients:

- Review this Guide with your doctor, pharmacist, or nurse.
- Ask questions!
- Make sure you understand what you need to do to receive Clozapine.
What is clozapine?

Clozapine is a prescription medicine to treat people with schizophrenia who have not responded to other medicines. Clozapine may also reduce the risk of suicidal behavior.

What is the most serious risk of clozapine treatment?

Clozapine can cause a blood condition (severe neutropenia), which can lead to serious infections and death. Neutropenia occurs when you have too few of a certain type of white blood cells called neutrophils. This makes it harder for your body to fight infections.

Why do I need to have blood tests?

Getting your blood tested is important because a low number of neutrophils may not cause any symptoms until you have an infection. Having a blood test helps your doctor know if you are more likely to get an infection.

You must have regular blood tests before you start taking clozapine and during your treatment. This test is called absolute neutrophil count (ANC). If the number of neutrophils, or ANC, is too low, you may have to stop clozapine. Your doctor will decide if or when it is safe to restart clozapine.

What are the symptoms of infection?

- Infection, including skin, throat, urinary tract, vaginal, pneumonia, or any other infection
- Fever or chills
- Sores or ulcers inside your mouth, gums, or on your skin
- Wounds that take a long time to heal
- Feel like you have the flu
- Pain or burning while urinating
- Unusual vaginal discharge or itching
- Abdominal pain
- Sores or pain in or around your rectal area
- Feel extremely weak or tired

If you have any of these symptoms, talk to your doctor right away.
A Guide for Patients and Caregivers: What You Need to Know about Clozapine and Neutropenia

What can I do to help reduce the risk of developing neutropenia?

✔️ Three important things you can do:
1. Have your blood tested as instructed by your doctor.
2. Tell your doctor about all the medicines you are taking (prescription and over-the-counter) and if you start a new medicine.
3. Tell your doctor right away if you get a fever, feel sick, or have any signs of infections.

What are the blood testing requirements for clozapine?

Get your Blood Tested
- Your doctor will give you an order to have blood tests done.
- You will need to get your blood tested on the following schedule or as directed by your doctor:
  - Weekly blood tests for the first 6 months you are taking clozapine
  - Every 2 weeks for the next 6 months if your ANC stays normal
  - Monthly after the first year if your ANC stays normal

Results
- If your ANC is too low, your doctor will schedule blood tests more frequently.

Stay on Clozapine
- The Clozapine REMS will keep track of your blood test results so your doctor and pharmacist know if it is safe to fill your clozapine prescription.

How do I receive my clozapine from the pharmacy?

Only certain pharmacies are allowed to provide you with clozapine. Your doctor will help you find a pharmacy.

Remember: You must get your blood tested before you can receive clozapine from your pharmacy!
What is the Clozapine Risk Evaluation and Mitigation Strategy (REMS)?

A REMS is a drug safety program that the U.S. Food and Drug Administration (FDA) can require for certain medicines with serious safety concerns. Drug companies and healthcare providers must take extra steps to make sure the benefits of using the drug are more than the risks. Clozapine has a REMS because treatment with clozapine may cause a blood condition (severe neutropenia), which can lead to serious infections and death.

Where can I get more information about clozapine?

If you would like more information, talk to your doctor or visit www.clozapinerems.com.

Report any side effects directly to the Clozapine REMS at 888-586-0758. You can also report negative side effects to the FDA at www.fda.gov/medwatch, or call 800-FDA-1088.
Clozapine and the Risk of Neutropenia:

A Guide for Pharmacists

This Guide discusses:

- What is the Clozapine REMS?
- Clozapine and the risk of severe neutropenia
- Treatment recommendations and patient absolute neutrophil count (ANC) monitoring
- Pharmacy requirements for the Clozapine REMS

Look for this symbol to point out changes to the Clozapine REMS.
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The Clozapine REMS

Clozapine is associated with severe neutropenia (absolute neutrophil count (ANC) less than 500/μL). The requirements to prescribe, dispense, and receive clozapine are incorporated into a single shared program called the Clozapine Risk Evaluation and Mitigation Strategy (REMS). A REMS is a strategy to manage known or potential risks associated with a drug or group of drugs and is required by the Food and Drug Administration (FDA) for clozapine to ensure that the benefits of the drug outweigh the risk of severe neutropenia.

The Clozapine REMS provides a centralized point of access:
1. For prescribers and pharmacies to certify before prescribing or dispensing clozapine
2. To enroll and manage patients on clozapine treatment

Clozapine is available by prescription as:
- Clozaril® (clozapine) tablets, for oral use
- Versacloz® (clozapine, USP) oral suspension
- Approved generic equivalents of these products

To minimize the risk of severe neutropenia associated with the use of clozapine, the Clozapine REMS includes the following key program requirements:

**Prescribers (who prescribe clozapine for outpatient use or initiate treatment for inpatients)**
- Must certify in the Clozapine REMS to prescribe clozapine
- Must enroll all patients in the Clozapine REMS
- Must provide a baseline ANC when enrolling a new patient
- Must order ANC testing for each of their clozapine patients according to the clozapine Prescribing Information
- Must verify each clozapine patient’s ANCs to the Clozapine REMS monthly, using the Patient Status Form (Each ANC value may be separately submitted, when obtained, using the ANC Lab Reporting Form)

**Outpatient Pharmacies**
- Must certify in the Clozapine REMS to dispense clozapine
- Must obtain a REMS Dispense Authorization (RDA) prior to dispensing a clozapine prescription.
  - For the first dispensing after enrollment, the RDA will verify that:
    - the pharmacy is certified
    - the patient is enrolled
    - the patient’s treatment is not interrupted or discontinued
  - For a subsequent dispensing, the RDA will verify that:
    - the pharmacy is certified
    - the patient is enrolled
    - a Patient Status Form has been completed in the last 37 days
      - the prescriber has authorized the continuation of treatment if one or more labs are missing
      - the prescriber has provided a Treatment Rationale if the most current ANC lab value is below the acceptable range
    - the patient’s treatment is not interrupted or discontinued
**Inpatient Pharmacies**
- Must certify in the Clozapine REMS to dispense clozapine
- Must obtain a REMS Dispense Authorization (RDA) before the initial dispensing of clozapine.
  
  For the first dispensing after enrollment, the RDA will verify that:
  - the pharmacy is certified
  - the patient is enrolled
  - the patient’s treatment is not interrupted or discontinued

  For a subsequent dispensing, the RDA will verify that:
  - the pharmacy is certified
  - the patient is enrolled
  - a Patient Status Form has been completed in the last 37 days
    - the prescriber has authorized the continuation of treatment if one or more labs are missing
    - the prescriber has authorized a Treatment Rationale if the most current ANC lab value is below the acceptable range
  - the patient’s treatment is not interrupted or discontinued

**Patients**
- Must be enrolled in the Clozapine REMS by a certified prescriber to receive clozapine
- Must comply with the ANC testing requirements
2 Absolute Neutrophil Count (ANC), Neutropenia, and Patient ANC Monitoring

What is Absolute Neutrophil Count (ANC)?

ANC is the laboratory parameter for monitoring patients for clozapine-induced neutropenia. Prescribers must submit the ANC before starting and during clozapine treatment.

ANC is usually available as a component of the complete blood count (CBC), including differential:

- ANC is more relevant to drug-induced neutropenia than white blood cell (WBC) count
- ANC may also be calculated using the following formula:

\[
\text{Absolute Neutrophil Count} = \frac{\text{Total WBC Count}}{\text{Total percentage of neutrophils obtained from the differential}}
\]

*Includes both banded and segmented neutrophils

Other granulocytes (basophils and eosinophils) contribute minimally to neutropenia and their measurement is not necessary.

What is the risk of severe neutropenia associated with clozapine?

Clozapine can cause severe neutropenia, which can lead to serious infections and death. Severe neutropenia occurs in a small percentage of patients taking clozapine.

- Severe neutropenia is defined as ANC less than 500/μL
- “Severe neutropenia” replaces the previous terms “severe leukopenia,” “severe granulocytopenia,” and “agranulocytosis”
- The risk appears greatest during the first 18 weeks of clozapine treatment
- The mechanism is not dose-dependent
- It is unclear if concurrent use of other drugs known to cause neutropenia increases the risk or severity of clozapine-induced neutropenia
- If clozapine is used concurrently with a medication(s) known to cause neutropenia:
  - Consider monitoring patients more closely than the treatment guidelines recommend, and
  - Consult with the treating oncologist in patients receiving concomitant chemotherapy

For a complete discussion of other risks, including other Boxed Warnings, please see the full Prescribing Information available at www.clozapinerems.com.
What is Benign Ethnic Neutropenia (BEN)?

BEN is a condition observed in certain ethnic groups whose average ANCs are lower than "standard" laboratory ranges for neutrophils. Because of this condition, patients who have been diagnosed with BEN have a separate ANC monitoring algorithm when treated with clozapine.

When enrolling a patient in the Clozapine REMS, identify if the patient has documented BEN, so the patient is monitored according to the correct ANC monitoring algorithm.

A few important things to know about patients with documented BEN:
- It is most commonly observed in individuals of African descent (approximate prevalence of 25-50%), 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. Consider a hematology consultation before starting or during clozapine treatment as necessary.

What are the treatment recommendations and monitoring requirements for patients taking clozapine?

Before starting treatment with clozapine, the baseline ANC must be:
- at least 1500/μL for the general population
- at least 1000/μL for patients diagnosed with BEN

During treatment, monitor ANC regularly as described in Table 1 and Table 2 below.

Patients may transition to less frequent ANC monitoring based on the number of weeks of continuous clozapine therapy and the patient’s ANCs.

During the first six months of treatment:
- Weekly ANC monitoring is required for all patients

During the second six months of treatment:
- Monitoring frequency can be reduced to every two weeks if the ANC remains in the normal range (ANC greater than or equal to 1500/μL for the general population, ANC greater than or equal to 1000/μL for patients with BEN)

After one year of treatment:
- If the patient's ANC continues to remain in the normal range, ANC monitoring may be reduced to monthly (every 4 weeks) thereafter.
The recommended ANC monitoring frequency for patients in the general population and patients who have documented BEN is shown in **Table 1** and **Table 2** below. The table also provides recommendations for monitoring patients who experience a decrease in ANC during the course of treatment.

**Table 1 - Recommended Monitoring Frequency and Clinical Decisions by ANC Level for the General Patient Population**

<table>
<thead>
<tr>
<th>ANC Level</th>
<th>Treatment Recommendation</th>
<th>ANC Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Range</td>
<td>- Initiate treatment&lt;br&gt; - If treatment interrupted:&lt;br&gt;   - &lt; 30 days, continue monitoring as before&lt;br&gt;  - ≥ 30 days, monitor as if new patient&lt;br&gt;  - Discontinuation for reasons other than neutropenia</td>
<td>- Weekly from initiation to six months&lt;br&gt;  - Every two weeks from 6 to 12 months&lt;br&gt;  - Monthly after 12 months&lt;br&gt;  - See Section 2.4 of the Prescribing Information</td>
</tr>
<tr>
<td>Mild Neutropenia (1000 - 1499/µL)*</td>
<td>- Continue treatment</td>
<td>- Three times weekly until ANC ≥ 1500/µL&lt;br&gt;  - Once ANC ≥ 1500/µL, return to patient’s last “Normal Range” ANC monitoring interval**</td>
</tr>
<tr>
<td>Moderate Neutropenia (500 - 999/µL)*</td>
<td>- Recommend hematology consultation&lt;br&gt;  - Interrupt treatment for suspected clozapine-induced neutropenia&lt;br&gt;  - Resume treatment once ANC normalizes to ≥ 1000/µL</td>
<td>- Daily until ANC ≥ 1000/µL, then:&lt;br&gt;  - Three times weekly until ANC ≥ 1500/µL&lt;br&gt;  - Once ANC ≥ 1500/µL, check ANC weekly for 4 weeks, then return to patient’s last “Normal Range” ANC monitoring interval**</td>
</tr>
<tr>
<td>Severe Neutropenia (&lt; 500/µL)*</td>
<td>- Recommend hematology consultation&lt;br&gt;  - Interrupt treatment for suspected clozapine-induced neutropenia&lt;br&gt;  - Do not rechallenge unless prescriber determines benefits outweigh risks</td>
<td>- Daily until ANC ≥ 1000/µL&lt;br&gt;  - Three times weekly until ANC ≥ 1500/µL&lt;br&gt;  - If patient rechallenged, resume treatment as a new patient under “Normal Range” monitoring once ANC ≥1500/µL</td>
</tr>
</tbody>
</table>

* Confirm all initial reports of ANC less than 1500/µL with a repeat ANC measurement within 24 hours
** If clinically appropriate
Table 2 - Recommended Monitoring Frequency and Clinical Decisions by ANC Level for Patients with BEN

<table>
<thead>
<tr>
<th>ANC Level</th>
<th>Treatment Recommendation</th>
<th>ANC Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal BEN Range</td>
<td>- Obtain at least two baseline ANC levels before initiating treatment</td>
<td>• Weekly from initiation to 6 months</td>
</tr>
<tr>
<td>(Established ANC baseline</td>
<td>- If treatment interrupted:</td>
<td>• Every 2 weeks from 6 to 12 months</td>
</tr>
<tr>
<td>≥1000/μL)</td>
<td>- &lt; 30 days, continue monitoring as before</td>
<td>• Monthly after 12 months</td>
</tr>
<tr>
<td></td>
<td>- ≥ 30 days, monitor as if new patient</td>
<td>• See Section 2.4 of the Prescribing Information</td>
</tr>
<tr>
<td></td>
<td>- Discontinuation for reasons other than neutropenia</td>
<td></td>
</tr>
<tr>
<td>BEN Neutropenia (500 - 999/μL)*</td>
<td>- Recommend hematology consultation</td>
<td>• Three times weekly until ANC ≥ 1000/μL or ≥ patient’s known baseline.</td>
</tr>
<tr>
<td></td>
<td>- Continue treatment</td>
<td>• 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**</td>
</tr>
<tr>
<td>BEN Severe Neutropenia (&lt; 500/μL)*</td>
<td>- Recommend hematology consultation</td>
<td>• Daily until ANC ≥ 500/μL</td>
</tr>
<tr>
<td></td>
<td>- Interrupt treatment for suspected clozapine-induced neutropenia</td>
<td>• Three times weekly until ANC ≥ patients baseline</td>
</tr>
<tr>
<td></td>
<td>- Do not rechallenge unless prescriber determines benefits outweigh risks</td>
<td>• If patient rechallenged, resume treatment as a new patient under “Normal Range” monitoring once ANC ≥1000/μL or at patient’s baseline</td>
</tr>
</tbody>
</table>

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

Can a patient continue clozapine treatment with an ANC less than 1000/μL?

For Patients in the General Population

Yes; prescribers may choose to continue clozapine treatment in patients with ANCs less than 1000/μL. However, prescribers should follow the treatment recommendations as noted in Table 1 and carefully determine if the benefits of continuing clozapine treatment outweigh the risks.

The recommendations to interrupt treatment are provided to ensure patient safety. If monitoring ANC and symptoms of infection is not done appropriately, patients with ANCs less than 1000/μL are at risk for developing complications of severe neutropenia, including serious infection and death.

For Patients with documented BEN

Yes; the Prescribing Information for clozapine recommends interrupting clozapine treatment for patients with BEN only when the ANC is less than 500/μL. No interruption in treatment is recommended for ANC 500-999/μL, although a hematology consultation is recommended.
If a patient develops a fever, how is clozapine treatment managed?

Generally, clozapine treatment should be interrupted as a precautionary measure in any patient who develops a fever of 38.5°C (101.3°F) or greater, and an ANC should be obtained. Fever is often the first sign of a neutropenic infection.

If fever occurs in any patient with an ANC less than 1000/μL, initiate appropriate neutropenia work-up and treatment for infection. Refer to Table 1 and Table 2 for ANC monitoring recommendations.

If any patient presents with evidence of fever and/or neutropenia, consider a hematology consultation.

How is clozapine discontinued for neutropenia?

The method of treatment discontinuation will vary depending on the patient’s most recent ANC result. Abrupt treatment discontinuation is necessary for moderate to severe neutropenia that the prescriber suspects is caused by clozapine. The prescriber may discontinue treatment by the methods listed below.

![Remember to submit the decision to discontinue clozapine for a patient to the Clozapine REMS. You can complete this in one of three ways: By signing in to the Clozapine REMS Website at www.clozapinerems.com By calling the Clozapine REMS Contact Center at 888-586-0758 By completing the “Patient Status” section of the Clozapine REMS Patient Status Form and faxing it to the Clozapine REMS at 800-878-5927](image)

How is a patient monitored if clozapine treatment is discontinued for neutropenia?

- Monitor ANC in any patient reporting a fever (temperature of 38.5°C or 101.3°F or greater) during the 2 weeks after discontinuation
- Monitor all patients carefully for the recurrence of psychotic symptoms and symptoms related to cholinergic rebound, such as profuse sweating, headache, nausea, vomiting, and diarrhea
- For abrupt clozapine discontinuation for a reason unrelated to neutropenia, continuation of the existing ANC monitoring is recommended for general population patients until their ANC is greater than or equal to 1500/μL and for patients with documented BEN until their ANC is greater than or equal to 1000/μL or above their baseline

After discontinuing clozapine, monitor ANC according to the recommendations in Table 3 as shown below.
Table 3 Recommended monitoring frequency when clozapine treatment is discontinued

<table>
<thead>
<tr>
<th>Moderate Neutropenia (500 to 999/μL)*</th>
<th>GENERAL POPULATION</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Daily until ANC ≥ 1000/μL, then</td>
</tr>
<tr>
<td></td>
<td>Three times weekly until ANC ≥ 1500/μL</td>
</tr>
<tr>
<td>Severe Neutropenia (less than 500/μL)*</td>
<td>GENERAL POPULATION</td>
</tr>
<tr>
<td></td>
<td>Daily until ANC ≥ 1000/μL, then</td>
</tr>
<tr>
<td></td>
<td>Three times weekly until ANC ≥ 1500/μL</td>
</tr>
<tr>
<td></td>
<td>BEN POPULATION</td>
</tr>
<tr>
<td></td>
<td>Daily until ANC ≥ 500/μL</td>
</tr>
<tr>
<td></td>
<td>Three times weekly until ANC ≥ patients established baseline</td>
</tr>
</tbody>
</table>

* Confirm all initial reports of ANC less than 1500/μL (ANC < 1000/μL for BEN patients) with a repeat ANC measurement within 24 hours.

Refer to Section 2.4 of the clozapine Prescribing Information for further information.

**Can a patient be rechallenged with clozapine?**

Yes; for some patients who experience, or have experienced, moderate clozapine-related neutropenia (ANC less than 1000/μL) or severe clozapine-related neutropenia (ANC less than 500/μL), the risk of serious psychiatric illness from discontinuing clozapine may be greater than the risk of rechallenge. This may be relevant for patients with severe schizophrenic illness who have no treatment option other than clozapine.

In making the decision to rechallenge a patient, consider:

- A hematology consult
- The ANC ranges defined in the Prescribing Information
- The patient’s medical and psychiatric history
- A discussion with the patient and his or her caregiver about the benefits and risks of clozapine rechallenge
- The severity and characteristics of the neutropenic episode

Refer to Section 2.5 in the clozapine Prescribing Information for more information on how to restart clozapine in patients who have discontinued clozapine.
**What types of pharmacies must be certified?**

All inpatient and outpatient pharmacies must certify in the Clozapine REMS to purchase and dispense clozapine. The requirements for outpatient pharmacies are different from the requirements for inpatient pharmacies. The different requirements are explained in the section, “How do I verify the patient is authorized to receive clozapine?”

An **inpatient pharmacy** is a pharmacy within a facility dispensing clozapine only to patients receiving inpatient medical care and other related services for surgery, acute medical conditions, or injuries (usually for a short-term illness or condition).

An **outpatient pharmacy** is a pharmacy that dispenses clozapine only to patients treated on an outpatient or chronic basis including, but not limited to, retail drug-stores, ambulatory care pharmacies, and pharmacies dispensing to long-term care, rehabilitation facilities, and prison systems.

The designated authorized representative for the pharmacy will complete the *Inpatient Pharmacy Enrollment Form* and/or the *Outpatient Pharmacy Enrollment Form*. This form is to certify a single inpatient or a single outpatient pharmacy location.

The authorized representative for the pharmacy or pharmacies can certify the pharmacy online or by fax. Certifying multiple pharmacy locations must be completed online.

**Who is an Authorized Representative?**

In general, an authorized representative for a pharmacy:

- Coordinates the activities required in the Clozapine REMS
- Establishes and implements processes and procedures to ensure compliance with the safe-use conditions required in the Clozapine REMS

Specific duties of an authorized representative are noted in the section, "What is the role of the pharmacy authorized representative in the Clozapine REMS?"

For a pharmacy with a single location, the authorized representative may be a:

- Pharmacy Manager, or
- Staff Pharmacist
Clozapine and the Risk of Neutropenia:  
A Guide for Pharmacists 

If your pharmacy has more than one pharmacy location and your organization would like to coordinate staff training and implement processes for all the pharmacies in your organization, the authorized representative may be a:  

- Director of Pharmacy Services, or  
- Corporate Executive overseeing Pharmacy Services

What is the role of the pharmacy authorized representative in the Clozapine REMS? 

Designate an authorized representative for your pharmacy. The authorized representative for every pharmacy must:

**Step 1: Certify in the Clozapine REMS by:**

- Reviewing Clozapine and the Risk of Neutropenia: A Guide for Pharmacists
- Successfully complete and submit the Knowledge Assessment for Pharmacies
- Complete and submit the Inpatient Pharmacy Enrollment Form and/or the Outpatient Pharmacy Enrollment Form

**Step 2: Ensure training for all relevant staff** involved in the dispensing of clozapine on the Clozapine REMS requirements using the Clozapine and the Risk of Neutropenia: A Guide for Pharmacists

Once a staff is trained on the Clozapine REMS requirements, the authorized representative may invite that staff to become enrolled in the Clozapine REMS. To invite a staff or an additional authorized representative, log into your account at [www.clozapinerems.com](http://www.clozapinerems.com). Select the Manage Personnel button, then select the Add Authorized Representative or Staff button and follow the steps.

**Step 3: Put processes and procedures in place** to verify an available, current ANC is within the acceptable range for patients enrolled but not authorized to receive the drug.

For patients enrolled but not authorized to receive clozapine, verify an available, current ANC is within the acceptable range through the processes and procedures established as a requirement of the Clozapine REMS, document and submit the ANC and the prescriber’s NPI to the Clozapine REMS and obtain authorization to dispense each prescription by contacting the Clozapine REMS program to verify the patient is now authorized to receive clozapine.

**Does a Pharmacy’s Certification Expire?**

A pharmacy’s certification does not expire. However, if a pharmacy’s authorized representative changes, the new authorized representative must certify the pharmacy in the REMS Program by reviewing Clozapine and the Risk of Neutropenia: A Guide for Pharmacists, successfully completing the Knowledge Assessment for Pharmacies and the Outpatient Pharmacy Enrollment Form and submitting both to the REMS Program.
How do I verify the patient is authorized to receive clozapine?

Before any pharmacy dispenses clozapine to a patient, you must obtain authorization from the Clozapine REMS in the form of a REMS Dispense Authorization (RDA).

What is a REMS Dispense Authorization (RDA)?

An RDA is an electronic code that indicates the Clozapine REMS has verified that all safe use conditions have been met.

For the first dispensing, the RDA will verify that:
- the pharmacy is certified
- the patient is enrolled
- the patient’s treatment is not interrupted or discontinued

For a subsequent dispensing, the RDA will verify that:
- the pharmacy is certified
- the patient is enrolled
- a Patient Status Form has been completed in the last 37 days
  - the prescriber has authorized the continuation of treatment if one or more labs are missing
  - the prescriber has provided a Treatment Rationale if the most current ANC lab value is below the acceptable range
  - the patient’s treatment is not interrupted or discontinue

Obtain an RDA in one of two ways:
- By using the Clozapine REMS Website at www.clozapinerems.com
- By calling the Clozapine REMS Contact Center at 888-586-0758
Outpatient Pharmacies

Certification

As part of certification in the Clozapine REMS, the authorized representative for your pharmacy must implement processes to comply with program requirements, which include how your pharmacy will ensure an RDA is obtained each time a clozapine prescription is dispensed.

Dispensing

Before you dispense clozapine to each patient, you must obtain an RDA by:

Step 1: Accessing the Clozapine REMS in one of two ways:
- Sign in to the Clozapine REMS Website at www.clozapinerems.com, or
- Call the Clozapine REMS Contact Center at 888-586-0758

Step 2: Providing the following information:
- Pharmacy Location Information
- Patient Name
- Patient Date of Birth
- Dispense Date
- NDC
- Days' Supply
- Quantity Dispensed

Step 3: Before issuing the RDA, the Clozapine REMS will verify the following for you:

For the first dispensing after patient enrollment:
- the pharmacy is certified
- the patient is enrolled
- the patient’s treatment is not interrupted or discontinued

For a subsequent dispensing:
- the pharmacy is certified
- the patient is enrolled
- a Patient Status Form has been completed in the last 37 days
  - the prescriber has authorized the continuation of treatment if one or more labs are missing
  - the prescriber has provided a Treatment Rationale if the most current ANC lab value is below the acceptable range
  - the patient's treatment is not interrupted or discontinue

Using a Dispense Rationale

If a Patient Status Form has not been completed within the last 37 days, a Dispense Rationale will be automatically presented to you. To use the Dispense Rationale, you must be in possession of a current ANC within an acceptable range for the patient.

Enter the prescriber's NPI number, the blood draw date, and the ANC value and select the 'Request Dispense Rationale' button.

Three Dispense Rationales may be used per patient per year.
Step 4: Once an RDA is obtained, you can dispense clozapine to the patient.
- You do not need to document the RDA on the prescription or in your pharmacy management system.
- If you do not receive an RDA, the Clozapine REMS will provide a message to explain why you are not authorized to dispense clozapine to the patient.

⚠️ Dispensing Information for All Outpatient Pharmacies

- The amount of clozapine that can be dispensed depends on when the patient’s next blood draw is scheduled to occur, according to the monitoring frequency requirements.
- Pharmacies should dispense enough medication to treat the patient with clozapine until the next blood draw/ANC or as directed by the prescriber.
- If you do not receive an RDA, you will receive a message explaining why you are not authorized to dispense clozapine to the patient.

How do I Reverse an RDA?

If a prescription is not dispensed to the patient and is returned to stock, the RDA must be reversed. To reverse an RDA, log into your account at www.clozapinerems.com and select the Reverse RDA button. Find the patient and follow the directions.

You may also reverse and RDA by calling the Clozapine REMS Contact Center at 888-586-0758.

RDA Fact Sheet for Outpatient Pharmacies

An RDA Fact Sheet for Outpatient Pharmacies has been developed as a reference to help outpatient pharmacy staff understand the possible outcomes of an RDA, and actions to be taken by the pharmacy for each outcome. The Fact Sheet also has information for the following:

1. How Do I Request a REMS Dispense Authorization?
2. How Do I Request a Dispense Rationale?
3. How Do I Submit ANC Labs?

The RDA Fact Sheet for Outpatient Pharmacies can be found online at www.clozapinerems.com.
Inpatient Pharmacies

Certification
As part of certification in the Clozapine REMS, the authorized representative for your pharmacy must implement processes to comply with program requirements, which include how your pharmacy will ensure an RDA is obtained before the first inpatient clozapine prescription is dispensed.

Dispensing

Before you dispense the first inpatient clozapine dose to each patient, you must obtain an RDA by:

**Step 1: Accessing the Clozapine REMS** in one of two ways:
- Sign into the website at [www.clozapinerems.com](http://www.clozapinerems.com), or
- Call the Clozapine REMS Contact Center at 888-586-0758

**Step 2: Providing the following information:**
- Pharmacy Location Information
- Patient Name
- Patient Date of Birth
- Dispense Date

**Step 3: Before issuing the RDA, the Clozapine REMS will verify** the following for you:
  For the first dispensing after patient enrollment:
  - the pharmacy is certified
  - the patient is enrolled
  - the patient’s treatment is not interrupted or discontinued
  For a subsequent dispensing:
  - the pharmacy is certified
  - the patient is enrolled
  - a Patient Status Form has been completed in the last 37 days
    - the prescriber has authorized the continuation of treatment if one or more labs are missing
    - the prescriber has provided a Treatment Rationale if the most current ANC lab value is below the acceptable range
    - the patient’s treatment is not interrupted or discontinue

Using a Dispense Rationale
If a Patient Status Form has not been completed within the last 37 days, a Dispense Rationale will be automatically presented to you. To use the Dispense Rationale, you must be in possession of a current ANC within an acceptable range for the patient.

Enter the blood draw date and the ANC value and select the ‘Request Dispense Rationale’ button.
Step 4: Once an RDA is obtained, you can dispense clozapine to the patient.

- You do not need to document the RDA on the prescription or in your pharmacy management system
- If you do not receive an RDA, the Clozapine REMS will provide a message to explain why you are not authorized to dispense clozapine to the patient

While the patient is hospitalized, we encourage reporting ANCs to the Clozapine REMS according to the patient’s monitoring frequency using one of the options below.

How Do I Submit ANC values Outside of the RDA Process?

Yes, ANC values can be submitted using the following options:

Option 1: Use the Clozapine REMS Website to:

1. Log in to your account at www.clozapinerems.com
2. Select the button ‘Submit ANC Lab’
3. Find the patient information and enter the ANC value and Blood Draw Date

Option 2: Document the ANC results on an ANC Lab Reporting Form and fax the completed form to 800-878-5927.

Option 3: Call the Clozapine REMS Contact Center at 888-586-0758.

How do I Reverse an RDA?

If a prescription is not dispensed to the patient and is returned to stock, the RDA must be reversed. To reverse an RDA, log into your account at www.clozapinerems.com and select the Reverse RDA button. Find the patient and follow the directions.

You may also reverse an RDA by calling the Clozapine REMS Contact Center at 888-586-0758.

RDA Fact Sheet for Inpatient Pharmacies

An RDA Fact Sheet for Inpatient Pharmacies has been developed as a reference to help inpatient pharmacy staff understand the possible outcomes of an RDA, and actions to be taken by the pharmacy for each outcome. The Fact Sheet also has information for the following:

1. How Do I Request a REMS Dispense Authorization?
2. How Do I Request a Dispense Rationale?
3. How Do I Submit ANC Labs?

The RDA Fact Sheet for Inpatient Pharmacies can be found online at www.clozapinerems.com.
## Reporting Adverse Events Associated with Clozapine

Report suspected adverse events directly to the Clozapine REMS Contact Center at 888-586-0758. You also may report adverse event information to the FDA MedWatch Reporting System by telephone at (800) FDA-1088 or by mail using Form 3500A, available at [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

## Clozapine REMS Information and Resources

Additional Clozapine REMS information and resources are available online at [www.clozapinerems.com](http://www.clozapinerems.com) or by calling the Clozapine REMS Contact Center at 888-586-0758.

### Glossary

<table>
<thead>
<tr>
<th><strong>Absolute neutrophil count (ANC):</strong></th>
<th>Laboratory parameter for monitoring patients for clozapine-induced neutropenia.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Benign Ethnic Neutropenia (BEN):</strong></td>
<td>A condition observed in certain ethnic groups whose average ANC is lower than “standard” laboratory ranges for neutrophils compared to the general population. Patients with documented BEN have a separate ANC monitoring algorithm when treated with clozapine.</td>
</tr>
<tr>
<td><strong>Dispense Rationale:</strong></td>
<td>The Clozapine REMS Program provides certified pharmacies with an opportunity to apply clinical judgment and continue to dispense clozapine to enrolled patients when a Patient Status Form has not been received and the pharmacist is in possession of a current ANC within an acceptable range for the patient.</td>
</tr>
<tr>
<td><strong>Inpatient pharmacy:</strong></td>
<td>A pharmacy within a facility dispensing clozapine only to patients receiving inpatient medical care and other related services for surgery, acute medical conditions or injuries (usually for a short-term illness or condition).</td>
</tr>
<tr>
<td><strong>Outpatient pharmacy:</strong></td>
<td>A pharmacy dispensing clozapine only to patients treated on an outpatient or chronic basis. This includes, but is not limited to, retail drugstores, ambulatory care pharmacies, and pharmacies dispensing to long-term care, rehabilitation facilities and prison systems.</td>
</tr>
</tbody>
</table>
REMS Dispense Authorization (RDA): An authorization given to pharmacies which reflects that the safe-use conditions for that patient have been met. The RDA is provided by the Clozapine REMS. For an outpatient pharmacy, the RDA verifies that the patient is enrolled, the pharmacy is certified, and that the patient is authorized to receive drug. For an inpatient pharmacy, the RDA verifies that the patient is enrolled, and the pharmacy is certified. This RDA permits dispensing of clozapine to the patient.

Treatment Rationale (TR): A justification used by a prescriber to allow a patient having moderate neutropenia (ANC 500-999/µL for the general population) or severe neutropenia (ANC < 500/µL for general population and patients with documented BEN) to continue treatment. Only prescribers can confirm that benefits of continuing clozapine treatment outweigh the risks of developing severe neutropenia.
Instructions
1. Complete Sections 1 and 2 below to ensure the Knowledge Assessment is associated with your program record.
2. Answer all questions in Section 3.
3. Fax the completed Knowledge Assessment for Pharmacies to the Clozapine REMS at 800-878-5927.

For real-time processing of this Knowledge Assessment, please go to www.clozapinerems.com.

1 Pharmacy Information (PLEASE TYPE OR PRINT)
Pharmacy Name: ____________________________
Organization NPI #: ______________________

Address: ____________________________

City: ____________________________ State: __________ Zip Code: __________

Phone: ____________________________ Ext. (opt): __________ Fax (opt): __________

2 Pharmacy Authorized Representative Information
First Name: ____________________________ MI (opt): ______ Last Name: __________

Email Address: ____________________________

Phone: ____________________________ Ext. (opt): __________ Fax (opt): __________

3 Knowledge Assessment
Please select the best answer for each of the following questions. All questions must be answered correctly to become certified.

Question 1
All clozapine products are only available under the single shared Clozapine REMS.
A. True
B. False

Question 2
Clozapine is associated with severe neutropenia, which can lead to serious infection and death.
A. True
B. False

Question 3
Severe neutropenia is defined as:
A. A white blood cell count (WBC) less than 2000/µL
B. An absolute neutrophil count (ANC) less than 1000/µL
C. An absolute neutrophil count (ANC) less than 500/µL
D. None of the above

Continued on next page
Question 4

Before initiating treatment with clozapine:
A. A baseline absolute neutrophil count (ANC) must be at least 1000/µL for a patient with documented benign ethnic neutropenia (BEN)
B. A baseline absolute neutrophil count (ANC) must be at least 1500/µL for a patient who is part of the general population (i.e., the patient does not have documented BEN)
C. A baseline absolute neutrophil count (ANC) is not necessary
D. Both A and B

Question 5

Before clozapine treatment initiation, a certified prescriber must:
A. Determine if the patient has documented BEN
B. Enroll the patient in the Clozapine REMS
C. Counsel the patient/caregiver about the risk of severe neutropenia
D. Order blood work to obtain an ANC
E. Review the ANC and submit it to the Clozapine REMS
F. All of the above

Question 6

Prescribers must submit the Patient Status Form monthly, to the Clozapine REMS, before the patient is authorized to be dispensed clozapine.
A. True
B. False

Question 7

Before each outpatient dispensing or before the first inpatient dispensing for a patient, the pharmacist must:
A. Verify the patient is enrolled in the Clozapine REMS
B. Verify the patient is authorized to receive drug
C. Obtain a REMS Dispense Authorization each time from the REMS
D. For patients enrolled but not authorized by the Clozapine REMS to receive clozapine, document and submit an available, current ANC that is within acceptable range and obtain a Dispense Rationale
E. All of the above

Question 8

How much clozapine can be dispensed?
A. A 30-day supply
B. A 90-day supply
C. As much as the patient wants or the insurance will pay for
D. It depends when the patient’s next blood draw is, according to the monitoring requirements. Dispense enough medication to treat the patient with clozapine until the next blood draw/ANC or as directed by the prescriber

Continued on next page
Question 9

Regarding patients with documented BEN, which of the following statements are true?

A. Patients with BEN have a different clozapine treatment algorithm and monitoring requirements
B. Patients with BEN are healthy and do not suffer from repeated severe infections
C. Patients with BEN are NOT at increased risk for developing clozapine-induced neutropenia
D. Before starting clozapine, additional evaluation may be needed to determine if baseline neutropenia is due to BEN. Hematology consultation may be necessary
E. All of the above statements are true

Question 10

If a new patient’s baseline ANC is within the normal range, how should the ANC monitoring schedule proceed?

A. Weekly from initiation to discontinuation of therapy
B. Weekly from initiation to 6 months; every 2 weeks from 6 to 12 months; monthly after 12 months
C. Monthly from initiation to discontinuation of therapy
D. No additional ANC monitoring is required if the patient’s baseline ANC is within the normal range

Question 11

If a patient’s ANC indicates mild neutropenia, which of the following statements is true?

A. ANC monitoring should be conducted three times weekly until ANC ≥ 1500/μL if the patient is part of the general population (i.e., if the patient does not have documented BEN)
B. Mild neutropenia is within the normal range for a patient with documented BEN
C. If the patient has documented BEN, ANC monitoring should be conducted: weekly from initiation to 6 months; every 2 weeks from 6 to 12 months; monthly after 12 months
D. All of the above

Question 12

If a patient’s ANC indicates moderate neutropenia, which of the following statements is true?

A. Treatment should be continued regardless of whether the patient is part of the general population or has documented BEN
B. If the patient is part of the general population (i.e., if the patient does not have documented BEN), interrupt therapy and conduct ANC monitoring: daily until ANC ≥ 1000/μL; three times weekly until ANC ≥ 1500/μL; weekly for 4 weeks; then return to the patient’s last "Normal Range" ANC monitoring interval
C. The ANC monitoring schedule is the same regardless of whether the patient is part of the general population or has BEN
D. None of the above

Continued on next page
Question 13

If a patient’s ANC indicates severe neutropenia, which of the following statements is true?

A. Treatment should be interrupted regardless of whether the patient is part of the general population or has BEN and a hematology consultation should be considered; resume treatment only if the prescriber determines that the benefits of clozapine therapy outweigh the risks

B. If the patient is part of the general population (i.e., if the patient does not have documented BEN), interrupt treatment and conduct ANC monitoring: daily until ANC ≥ 1000/µL; three times weekly until ANC ≥ 1500/µL

C. The patient may still be rechallenged with clozapine at the discretion of the prescriber

D. All of the above

Required

Signature

X

Date: / /
Patient Status Form

Instructions

Assess the patient by obtaining complete blood counts, including the absolute neutrophil count (ANC), as described in the Prescribing Information. Record the ANC data on this form.

You can complete this form online at www.clozapinerems.com or fax it to the Clozapine REMS Contact Center at 1-800-878-5927.

This form must be completed monthly for each patient continuing treatment with clozapine. Please submit page 1 and any pages that apply to your patient’s monitoring frequency.

This form may also be used to:
- Interrupt, Discontinue, or Resume Treatment
- Designate the patient as a Benign Ethnic Neutropenia patient
- Create a Treatment Rationale when the patient’s ANC level is < 1000/μL for a general population patient or < 500/μL for a BEN patient
- Designate the patient as a Hospice patient

This form can be used by both a prescriber and prescriber designee. The following activities require the signature of a certified prescriber:
- Designating a patient as a Hospice Care patient
- Designating a patient as a Benign Ethnic Neutropenia patient
- Authorizing the continuation of therapy if one or more required labs are missing
- Creating a Treatment Rationale for a patient

By submitting this form, you are authorizing this patient to continue treatment on clozapine, unless Interrupt Treatment or Discontinue Treatment is selected.

Prescriber Information (* Indicates a Required Field)

<table>
<thead>
<tr>
<th>First Name*</th>
<th>Last Name*</th>
<th>Individual NPI #*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phone</td>
<td>Email Address</td>
<td>Fax</td>
</tr>
</tbody>
</table>

Prescriber Designee Information (* Indicates a Required Field if form is completed by a Prescriber Designee)

<table>
<thead>
<tr>
<th>First Name*</th>
<th>Last Name*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phone</td>
<td>Email Address</td>
</tr>
</tbody>
</table>

Patient Information (* Indicates a Required Field)

<table>
<thead>
<tr>
<th>First Name*</th>
<th>Last Name*</th>
<th>REMS Patient ID</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of Birth: YYYY/MM/DD</td>
<td>Zip Code</td>
<td>Gender: [ ] Male [ ] Female [ ] Other</td>
</tr>
</tbody>
</table>

Patient Status (* Indicates a Required Field)

1. Are you monitoring the patient as recommended in the Prescribing Information?*  
   [ ] Yes  [ ] No

2. What is the patient’s current monitoring frequency?*  
   [ ] 3 times a week  [ ] Every 2 weeks  [ ] Weekly  [ ] Monthly

3. Change the patient’s monitoring frequency to*:  
   [ ] 3 times a week  [ ] Every 2 weeks  [ ] No Change to the Monitoring Frequency  [ ] Weekly  [ ] Monthly

4. Did the patient experience any adverse event(s) due to clozapine-induced neutropenia (e.g. infection)?*  
   [ ] No  [ ] Yes → If yes, please provide a phone number where you may be reached by the Clozapine REMS Contact Center for additional information related to this event: __________.

Hospice Care patient designation. This section must be completed by the prescriber. The prescriber must sign below.

For hospice patients (i.e. terminally ill patients with an estimated life expectancy of six months or less), the prescriber may reduce the frequency of submitting a Patient Status Form to once every 6 months after a discussion with the patient and his/her caregiver. To change the frequency of submitting a Patient Status Form to once every 6 months for a hospice patient, the prescriber must sign below.

By signing below, I attest that the above is a hospice care patient.

Prescriber Signature: __________________________  Date (MM/DD/YYYY): _____________

Benign Ethnic Neutropenia (BEN) patient designation. This section must be completed by the prescriber. The prescriber must sign below.

A BEN patient designation provides a separate ANC monitoring algorithm for the patient. The BEN designation is a permanent status.

By signing below, I attest that the above is a patient with documented benign ethnic neutropenia.

Prescriber Signature: __________________________  Date (MM/DD/YYYY): _____________

Continue to the next pages to provide ANC Lab Data

Reference ID: 4886777
# Patient Status Form

**Reporting ANC Lab Data**

Instructions for entering ANC lab data on the following pages:

1. Locate the section below that aligns with the patient’s current monitoring frequency
2. Enter the blood draw date and the ANC range in the appropriate patient population (general or BEN) column or enter the ANC value.
3. If a lab is missing, select the reason for missing the lab. Note: If one or more labs are missing, the prescriber is required to authorize the continuation of therapy by providing a signature and date.
4. Report of an ANC lab value indicating moderate (general population) or severe neutropenia (general or BEN population) requires treatment to be interrupted or discontinued or the creation of a Treatment Rationale by the prescriber unless a more recent ANC lab value is provided that is $\geq 1000/\muL$ for a general population patient or $\geq 500/\muL$ for a BEN population patient.

## Weekly Monitoring Frequency (Enter data for the last four weekly blood draws for this patient)

<table>
<thead>
<tr>
<th>Blood Draw Date:</th>
<th>General Patient Population</th>
<th>BEN Patient Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>MM/DD/YYYY</td>
<td>□ Normal Range (≥ 1500/μL)</td>
<td>□ Normal BEN Range (≥ 1000/μL)</td>
</tr>
<tr>
<td></td>
<td>□ Mild Neutropenia (1000 to 1499/μL)</td>
<td>□ BEN Neutropenia (500 to 999/μL)</td>
</tr>
<tr>
<td></td>
<td>□ Moderate Neutropenia (500 to 999/μL)</td>
<td>□ BEN Severe Neutropenia (&lt; 500/μL)</td>
</tr>
<tr>
<td></td>
<td>□ Severe Neutropenia (&lt; 500/μL)</td>
<td></td>
</tr>
</tbody>
</table>

1 Prescriber signature is required to authorize the continuation of therapy if one or more labs are missing.

2 Interrupt / Discontinue treatment or create a Treatment Rationale.

**Prescriber Signature:**

**Date (MM/DD/YYYY):**

---

**Patient Treatment Status**

Complete this section to interrupt, discontinue, or resume treatment for this patient. No selection indicates the patient may continue treatment.

- [ ] Interrupt Treatment
- [ ] Discontinue Treatment
- [ ] Resume Treatment

**Treatment Rationale (if required) (Prescriber Signature required below)**

Complete this section to continue treatment if the patient has moderate neutropenia (ANC 500-999/μL for the general population) or severe neutropenia (ANC<500/μL for general population and patients with benign ethnic neutropenia), check and sign below:

- [ ] Benefits of continuing clozapine treatment outweigh the risk of neutropenia.
  
  Until (MM/DD/YYYY) _______________ (not to exceed 6 months)

**Prescriber Signature:**

**Date (MM/DD/YYYY):**

Continue to the next page for additional monitoring frequencies

---

**Reference ID:** 4886777

**Page 2 of 5**
### Every 2 Weeks Monitoring Frequency (Enter data for the last two every two weeks blood draws for this patient)

<table>
<thead>
<tr>
<th>Blood Draw Date: MM/DD/YYYY</th>
<th>General Patient Population</th>
<th>BEN Patient Population</th>
<th>ANC (per µL):</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reason for missing lab¹:</td>
<td>□ Normal Range (≥ 1500/µL)</td>
<td>□ Normal BEN Range (≥ 1000/µL)</td>
<td>or</td>
</tr>
<tr>
<td>□ Patient Refused</td>
<td>□ Mild Neutropenia (1000 to 1499/µL)</td>
<td>□ BEN Neutropenia (500 to 999/µL)</td>
<td></td>
</tr>
<tr>
<td>□ Clinician discretion</td>
<td>□ Moderate Neutropenia (500 to 999/µL)²</td>
<td>□ BEN Severe Neutropenia (&lt; 500/µL)²</td>
<td></td>
</tr>
<tr>
<td>Extrinsic factors</td>
<td>□ Severe Neutropenia (&lt; 500/µL)²</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Blood Draw Date: MM/DD/YYYY</th>
<th>General Patient Population</th>
<th>BEN Patient Population</th>
<th>ANC (per µL):</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reason for missing lab¹:</td>
<td>□ Normal Range (≥ 1500/µL)</td>
<td>□ Normal BEN Range (≥ 1000/µL)</td>
<td>or</td>
</tr>
<tr>
<td>□ Patient Refused</td>
<td>□ Mild Neutropenia (1000 to 1499/µL)</td>
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<td></td>
</tr>
<tr>
<td>□ Clinician discretion</td>
<td>□ Moderate Neutropenia (500 to 999/µL)²</td>
<td>□ BEN Severe Neutropenia (&lt; 500/µL)²</td>
<td></td>
</tr>
<tr>
<td>Extrinsic factors</td>
<td>□ Severe Neutropenia (&lt; 500/µL)²</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

¹ Prescriber signature is required to authorize the continuation of therapy if one or more labs are missing.
² Interrupt / Discontinue treatment or create a Treatment Rationale.

**Prescriber Signature:**

**Date (MM/DD/YYYY):**

### Patient Treatment Status

Complete this section to interrupt, discontinue, or resume treatment for this patient. No selection indicates the patient may continue treatment.

- [ ] Interrupt Treatment
- [ ] Discontinue Treatment
- [ ] Resume Treatment

### Treatment Rationale (If Required) (Prescriber Signature required below)

*Complete this section to continue treatment if the patient has moderate neutropenia (ANC 500-999/µL for the general population) or severe neutropenia (ANC<500/µL for general population and patients with benign ethnic neutropenia), check and sign below:*

- [ ] Benefits of continuing clozapine treatment outweigh the risk of neutropenia.
- [ ] Until (MM/DD/YYYY) ________________ (not to exceed 6 months)

**Prescriber Signature:**

**Date (MM/DD/YYYY):**

### Monthly Monitoring Frequency (Enter data for the last monthly blood draw for this patient)

<table>
<thead>
<tr>
<th>Blood Draw Date: MM/DD/YYYY</th>
<th>General Patient Population</th>
<th>BEN Patient Population</th>
<th>ANC (per µL):</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reason for missing lab¹:</td>
<td>□ Normal Range (≥ 1500/µL)</td>
<td>□ Normal BEN Range (≥ 1000/µL)</td>
<td>or</td>
</tr>
<tr>
<td>□ Patient Refused</td>
<td>□ Mild Neutropenia (1000 to 1499/µL)</td>
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<tr>
<td>Extrinsic factors</td>
<td>□ Severe Neutropenia (&lt; 500/µL)²</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

¹ Prescriber signature is required to authorize the continuation of therapy if one or more labs are missing.
² Interrupt / Discontinue treatment or create a Treatment Rationale.

**Prescriber Signature:**

**Date (MM/DD/YYYY):**

### Patient Treatment Status

Complete this section to interrupt, discontinue, or resume treatment for this patient. No selection indicates the patient may continue treatment.

- [ ] Interrupt Treatment
- [ ] Discontinue Treatment
- [ ] Resume Treatment

### Treatment Rationale (If Required) (Prescriber Signature required below)

*Complete this section to continue treatment if the patient has moderate neutropenia (ANC 500-999/µL for the general population) or severe neutropenia (ANC<500/µL for general population and patients with benign ethnic neutropenia), check and sign below:*

- [ ] Benefits of continuing clozapine treatment outweigh the risk of neutropenia.
- [ ] Until (MM/DD/YYYY) ________________ (not to exceed 6 months)

**Prescriber Signature:**

**Date (MM/DD/YYYY):**

Continue to the next page for additional monitoring frequencies
<table>
<thead>
<tr>
<th>Blood Draw Date:</th>
<th>General Patient Population</th>
<th>BEN Patient Population</th>
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<td>□ BEN Neutropenia (500 to 999/µL)</td>
</tr>
<tr>
<td></td>
<td>□ Clinician discretion</td>
<td>□ BEN Severe Neutropenia (&lt; 500/µL)²</td>
</tr>
<tr>
<td></td>
<td>□ Extrinsic factors (e.g., weather, transportation issues)</td>
<td></td>
</tr>
<tr>
<td>Blood Draw Date:</td>
<td>General Patient Population</td>
<td>BEN Patient Population</td>
</tr>
<tr>
<td>MM / DD / YYYY</td>
<td>□ Normal Range (≥ 1500/µL)</td>
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<td>Blood Draw Date:</td>
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</tr>
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<td>MM / DD / YYYY</td>
<td>□ Normal Range (≥ 1500/µL)</td>
<td>□ Normal BEN Range (≥ 1000/µL)</td>
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</tr>
<tr>
<td></td>
<td>□ Extrinsic factors</td>
<td></td>
</tr>
</tbody>
</table>

 Continued on next page
### Patient Status Form

#### Blood Draw Date:

**General Patient Population**
- Normal Range (≥ 1500/μL)
- Mild Neutropenia (1000 to 1499/μL)
- Moderate Neutropenia (500 to 999/μL)
- Severe Neutropenia (< 500/μL)

**BEN Patient Population**
- Normal BEN Range (≥ 1000/μL)
- BEN Neutropenia (500 to 999/μL)
- BEN Severe Neutropenia (< 500/μL)

**ANC (per μL):** or **ANC (per μL):**

#### Reason for missing lab¹:
- Patient Refused
- Clinician discretion
- Extrinsic factors

---

1 Prescriber signature is required to authorize the continuation of therapy if one or more labs are missing.

2 Interrupt / Discontinue treatment or create a Treatment Rationale.

#### Prescriber Signature: __________________________ Date (MM/DD/YYYY): __________________________

#### Patient Treatment Status

Complete this section to interrupt, discontinue, or resume treatment for this patient. No selection indicates the patient may continue treatment.
- [ ] Interrupt Treatment
- [ ] Discontinue Treatment
- [ ] Resume Treatment

#### Treatment Rationale (if Required) (Prescriber Signature required below)

Complete this section to continue treatment if the patient has moderate neutropenia (ANC 500-999/μL for the general population) or severe neutropenia (ANC<500/μL for general population and patients with benign ethnic neutropenia). Check and sign below:

- [ ] Benefits of continuing clozapine treatment outweigh the risk of neutropenia.

Until (MM/DD/YYYY) ________________ (not to exceed 6 months)

Prescriber Signature: __________________________ Date (MM/DD/YYYY): __________________________

Reference ID: 4886777
1. This form may be used by:
   a. certified prescribers and their designees to submit an ANC Lab outside of the monthly reporting requirement (using the Patient Status Form), and
   b. certified pharmacies to submit an ANC Lab.

2. A reported ANC Lab that is < 1000/µL for a general population patient or < 500/µL for a BEN patient will cause the patient’s treatment to be interrupted until:
   - The patient’s prescriber determines that the benefits of continuing clozapine outweigh the risk of neutropenia; or
   - A more recent ANC lab value is provided that is ≥ 1000/µL for a general population patient or ≥ 500/µL for a BEN population patient

3. Submission of an ANC Lab Reporting Form is not a substitute for the prescriber’s requirement to document and submit ANC results, the monitoring frequency, and appropriateness for continuing treatment monthly using the monthly Patient Status Form.

### Patient Information (* Indicates a Required Field)

<table>
<thead>
<tr>
<th>Field</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>First Name*</td>
<td></td>
</tr>
<tr>
<td>Last Name*</td>
<td></td>
</tr>
<tr>
<td>Date of Birth*</td>
<td>MM/DD/YYYY</td>
</tr>
<tr>
<td>REMS Patient ID:</td>
<td></td>
</tr>
<tr>
<td>Zip Code:</td>
<td></td>
</tr>
<tr>
<td>Gender:</td>
<td></td>
</tr>
<tr>
<td>□ Male</td>
<td></td>
</tr>
<tr>
<td>□ Female</td>
<td></td>
</tr>
<tr>
<td>□ Other</td>
<td></td>
</tr>
</tbody>
</table>

### Reporter Information (* Indicates a Required Field)

<table>
<thead>
<tr>
<th>Field</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>First Name*</td>
<td></td>
</tr>
<tr>
<td>Last Name*</td>
<td></td>
</tr>
<tr>
<td>Phone*</td>
<td></td>
</tr>
</tbody>
</table>

### Prescriber's Individual NPI #: or Pharmacy's Organizational NPI #: (Required Field)

### ANC Lab (Lab draw date required, enter either a range or the ANC for General Population or BEN Population)

<table>
<thead>
<tr>
<th>Blood Draw Date</th>
<th>General Patient Population</th>
<th>BEN Patient Population</th>
<th>ANC (µL):</th>
</tr>
</thead>
<tbody>
<tr>
<td>MM/DD/YYYY</td>
<td>□ Normal Range (≥ 1500/µL)</td>
<td>□ Normal BEN Range (≥ 1000/µL)</td>
<td>or</td>
</tr>
<tr>
<td></td>
<td>□ Mild Neutropenia (1000 to 1499/µL)</td>
<td>□ BEN Neutropenia (500 to 999/µL)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>□ Moderate Neutropenia (500 to 999/µL)</td>
<td>□ BEN Severe Neutropenia (&lt; 500/µL)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>□ Severe Neutropenia (&lt; 500/µL)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Re-certify and Re-enroll Patients Now

Dear Healthcare Provider,

The Clozapine REMS requirements are changing due to a recently approved modification. New Clozapine Requirements will be implemented November 15, 2021. Prescribers and patients who are not re-certified or re-enrolled after this time will not have access to clozapine.

- **Re-certify in the Clozapine REMS** in order to prescribe clozapine for outpatient use and/or initiate treatment for inpatients.
- **Re-enroll patients** continuing on clozapine treatment to avoid a break in patient treatment.
- **Re-certification of prescribers and their designees, and re-enrollment of patients must be done with the revised materials.** To do this, you may access the new clozapine REMS website **beginning August 16, 2021:**
  - Go to [www.clozapinerems.com](http://www.clozapinerems.com).
  - Click on the link in the **Important Program Update**. You will be taken to the modified Clozapine REMS website.
  - Prescribers must create new login credentials.
  - Click on Log-in | Register tab. These credentials will only work on the modified Clozapine REMS.
  - Prescribers must first review the Prescriber Training, complete and submit the Knowledge Assessment and Prescriber Enrollment Form to become re-certified.
  - Then re-enroll your patients using the Patient Enrollment Form.

- **A Transition Contact Center** is available at 888-586-0758 to support re-certification, re-enrollment activities and to answer questions.

- **After launch of the modified clozapine REMS on November 15, 2021, a NEW Patient Status Form** must be submitted monthly. The Patient Status Form documents the patient’s ANC results, monitoring frequency, and appropriateness to continue treatment.
  - Continue monitoring **existing patients** according to their current monitoring schedule using the ANC Lab Reporting Form prior to November 15, 2021. All existing patients will need to be re-enrolled in the new program by November 15, 2021.
All new patients starting **clozapine** between now and November 15, 2021 must be enrolled in both the current program and the new program.

- See [Fact Sheet: What's Changed in the Clozapine REMS for Prescribers](#) for more details on these and other changes to the program.

**Re-certify and re-enroll your patients prior to November 15th to avoid delays in patient treatment!**

**Questions?** Contact the Clozapine REMS Transition Call Center at **1-888-586-0758**.
TO: [Professional Society]

SUBJECT: Request to share important Clozapine REMS changes with members

PREVIEW TEXT: Changes in Requirements, Re-certification Needed in Clozapine REMS

Dear Professional Society,

A modification to Clozapine REMS has been recently approved and will be launched in November 15, 2021. We are asking for your help in sharing this important information with your members as there are significant changes to the requirements of the program.

- Prescribers must re-certify in the new Clozapine REMS in order to prescribe clozapine for outpatient use and/or initiate treatment for inpatients after November 15, 2021.
- Prescribers and Prescriber Designees can start re-certifying on August 16, 2021.
- Prescribers and Prescriber Designees must also re-enroll patients continuing on clozapine treatment. Patients can be re-enrolled starting August 16, 2021.

We have included a Drop In Summary (attached) of information to help with disseminating the important changes to the clozapine REMS, actions that prescribers must take to continue to provide clozapine treatment, and where to go to find more information.

We have also included a Fact Sheet: What’s Changed in the Clozapine REMS for Prescribers for more details on these and other changes to the program.

Please encourage your members to re-certify and re-enroll their patients prior to Nov 15th to avoid delays in patient treatment!

We thank you for your assistance.

Sincerely,

Clozapine REMS
Drop In Summary – Prescriber

Clozapine REMS Changes are Coming in November

On November 15, 2021, the Clozapine REMS will implement changes to the program requirements.

Prescriber Re-Certification and Patient Re-enrollment Required

- Prescribers will need to re-certify in the Clozapine REMS and re-enroll their patients to continue to prescribe clozapine for outpatient use and/or initiate treatment for inpatients after November 15, 2021.
- Prescriber designees must also re-enroll. Prescriber designees may re-enroll patients.
- To re-certify, prescribers must read the revised training, successfully complete the knowledge assessment and complete a new enrollment form.
  - Go to the current www.clozapineREMS.com and look for Important Program Update or pop-up message with information and link to revised Clozapine REMS platform.
  - Only the revised prescriber and patient enrollment forms will be accepted.
  - A Transition Contact Center is available at 888-586-0758 to support re-certification, re-enrollment activities and to answer questions.

REMS Requirement Changes

- Beginning November 15, 2021, a new Patient Status Form will now document patient monitoring for all outpatients. Although patient monitoring must continue per the Prescribing Information, the reporting on the Patient Status Form must be submitted monthly. The Patient Status Form documents the patient’s ANC results, monitoring frequency, and appropriateness to continue treatment.
  - Continue to monitor existing patients according to the current REMS requirements prior to the November 15, 2021 launch of the new Clozapine REMS Program. All existing patients will need to be re-enrolled in the new program by November 15, 2021.
  - All new patients starting clozapine between now and November 15, 2021, must be enrolled in both the current program and the new program.

- A new Clozapine REMS website platform will be available to monitor and track patients with a personalized online dashboard. This new website platform also has all the new materials prescribers will need to re-certify and re-enroll patients and is available at the new Clozapine REMS website.
- A Fact Sheet titled “What’s Changed in the Clozapine REMS for Prescribers?” explains the differences between the current and modified Clozapine REMS program.

Key Dates:

- August 2, 2021- The new contact center will be available to answer questions for stakeholders at 888-586-0758.
- August 16, 2021- All re-certification and re-enrollment for all stakeholders begins.
- November 15, 2021- New Clozapine REMS is launched.

Re-certify and re-enroll your patients prior to November 15th to avoid delays in patient treatment!
Switch System will be removed November 15, 2021; Re-certification required

Dear Authorized Representative,

The Clozapine REMS requirements are changing due to a recently approved modification. New Clozapine requirements will be implemented on November 15, 2021.

Starting November 15, 2021

- The current “switch” pharmacy management system is being removed. A REMS dispense authorization will only be provided by accessing either the modified Clozapine REMS website platform or the Clozapine REMS Call Center by phone.
- Only pharmacies with Authorized Representatives re-certified in the Clozapine REMS will be able to dispense clozapine.
- New processes and procedures may need to be put in place for your pharmacy to be able to continue dispensing clozapine.

Authorized Representatives must re-certify for your pharmacy to continue to dispense clozapine. You may re-certify beginning August 16, 2021. In order for an individual pharmacist to re-enroll in the Clozapine REMS, the certified Authorized Representative will need to invite the pharmacist to enroll in the program using a valid email address.
- Large chain pharmacies may call the Clozapine REMS Contact Center at 1-888-586-0758 to arrange for a bulk upload of stores and staff.

Starting August 16, 2021

- Re-certification will open August 16th at the new Clozapine REMS Website. To reach this new clozapine REMS website:
  - Go to www.clozapinerems.com.
  - Click on the link in the Important Program Update. You will be taken to the new Clozapine REMS website.
  - Authorized Representatives must create new log-in credentials.
Click on **Log-in | Register** tab. These credentials will only work on the modified Clozapine REMS website.

Authorized Representatives must first review the Pharmacy Training, complete and submit the Knowledge Assessment and Pharmacy Enrollment Form to become re-certified.

- Additionally, the Clozapine REMS Transition Call Center will be available on August 2, 2021 to help guide you through the re-certification process at 1-888-586-0758.
- Authorized Representatives must also train pharmacy staff using new materials and send staff an invitation to re-enroll after they are trained.
- See Fact Sheet: What’s Changed in the Clozapine REMS for Pharmacies for more details on these and other changes to the program.

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**Re-certify prior to November 15th to avoid delays in patient treatment!**

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**Questions?**

The Clozapine REMS Transition Call Center at **1-888-586-0758** can answer any questions you may have beginning August 2nd.

Signed,

CPMG
TO: [Professional Society]

SUBJECT: Request to share important Clozapine REMS changes with members

PREVIEW TEXT: “Switch” system removal from Clozapine REMS; Re-certification needed [for email version only]

Dear Professional Society,

A modification to the Clozapine REMS has been recently approved and will be launched on November 15, 2021. We are asking for your help in sharing this important information with your members as there are significant changes to the program.

The “switch” system is being removed as a way to verify clozapine dispensing. Pharmacists will now need to go to www.clozapineREMS.com or call the Clozapine REMS Contact Center to verify information and obtain a REMS dispense authorization to dispense clozapine. New processes and procedures may need to be put in place for pharmacies to be able to continue to dispense clozapine.

Pharmacy Authorized Representatives will also need to re-certify in the Clozapine REMS.

We have included a Drop In Summary (attached) of information to help with disseminating the important changes to the Clozapine REMS, actions that pharmacies must take to continue to dispense clozapine, and where to go to find more information.

We have also included a Fact Sheet: What’s Changed in the Clozapine REMS for Pharmacies for more details on these and other changes to the program.

Please encourage your members to re-certify prior to Nov 15th to avoid delays in patient treatment!

We thank you for your assistance.

Sincerely,

Clozapine REMS
Drop In Summary - Pharmacy

Clozapine REMS Changes are Coming in November

Pharmacy System Changes

- On November 15, 2021, a new Clozapine REMS will be launched with changes to the program requirements.
  - Beginning November 15, 2021, the current “switch” system or pharmacy management system that is currently used as an option to verify a dispense authorization will be removed. New processes and procedures may need to be put in place for your pharmacy to be able to continue dispensing clozapine.
  - Pharmacists will need to go to www.clozapineREMS.com or call the Clozapine Call Center to verify information and obtain a REMS dispense authorization to dispense clozapine.
  - A Fact Sheet titled “What’s Changed in the Clozapine REMS For Pharmacies?” explains the differences between the current and modified Clozapine REMS program and is available at the new Clozapine REMS website.

Authorized Representative Re-certification Required

- Pharmacy Authorized Representatives will need to re-certify in the new Clozapine REMS for the pharmacy to be able to dispense clozapine.
- Authorized Representatives must also train pharmacy staff with the new training materials.
- All pharmacists who will be obtaining a REMS dispense authorization will need to be enrolled or re-enrolled in order to dispense clozapine.
- A new Clozapine REMS website platform will be available to track patients with a pharmacy dashboard.
- To re-certify, Authorized Representatives must read the revised training, successfully complete the knowledge assessment and complete a new enrollment form.
  - Go to current www.clozapineREMS.com and look for Important Program Update or pop-up message with information and link to revised Clozapine REMS platform.
  - Only the revised pharmacy enrollment forms will be accepted.
  - The Clozapine REMS Transition Call Center will be available on August 2, 2021 to help guide you through the re-certification process at 888-586-0758.
  - Large chain pharmacies may call the Clozapine REMS Contact Center at 888-586-0758 to arrange for a bulk upload of stores and staff.

Key Dates:

- August 16, 2021- Authorized Representatives can begin to re-certify.
- November 15, 2021- New Clozapine REMS is launched.

Re-certify prior to November 15th to avoid delays in patient treatment!
ACTION NEEDED: Changes to the Clozapine REMS

Subject:  
- Current wholesalers/distributors must re-enroll in the Clozapine REMS
- Program changes effective November 15, 2021.
- Request assistance with informing pharmacies of changes

Dear Wholesaler/Distributor:

The Clozapine REMS requirements and REMS Administrator are changing. As a result, you will need to take action and re-enroll in order to continue distributing clozapine.

Starting November 15, 2021, you may only distribute clozapine when:

1. You re-enroll in the modified Clozapine REMS as a distributor through the Clozapine REMS,
2. The requesting pharmacy is certified in the modified Clozapine REMS, and
3. You verify the pharmacy’s certification through the Clozapine REMS.

Please complete and return the enclosed Wholesaler-Distributor Registration Form by faxing it to 800-878-5927 by November 15, 2021 to ensure you may continue to distribute in the modified Clozapine REMS. Once your re-enrollment is complete, you will be contacted to coordinate receiving the new daily pharmacy eligibility file.

In addition, the Clozapine REMS Sponsors request your assistance in preparing pharmacies for the modified Clozapine REMS. Between the dates of August 15, 2021 and December 31, 2021, please provide copies of the enclosed Pharmacy Letter and Fact Sheet: What’s Changed with the Clozapine REMS Program for Pharmacies to any pharmacy that orders clozapine.

For additional information related to the Clozapine REMS and recent program modifications, please call 1-888-586-0758.

Sincerely,

Clozapine REMS
Starting November 15, 2021, requirements to the Clozapine REMS will change.

### What are the important changes for prescribers and their designees?

#### During Treatment

<table>
<thead>
<tr>
<th>Previous Requirement</th>
<th>New Requirement</th>
</tr>
</thead>
</table>
| Using the *ANC Lab Reporting Form*, submit ANC according to the patient’s monitoring frequency on file with the Clozapine REMS as described in the Monitoring Schedule of the Prescribing Information.  
  - For weekly monitoring frequency, ANC must be submitted to the Clozapine REMS Program within 7 days of the lab draw date.  
  - For every two weeks monitoring frequency, ANC must be submitted to the Clozapine REMS Program within 15 days of the lab draw date.  
  - For monthly monitoring frequency, ANC must be submitted to the Clozapine REMS Program within 31 days of the lab draw date. | Monthly, using the *new Patient Status Form*, document the patient’s ANC results, the monitoring frequency, and appropriateness for continuing treatment and submit to the Clozapine REMS. The prescriber must authorize the continuation of therapy if one or more ANC is missing for the month.  
  Individual ANCs may still be submitted when obtained by completing and submitting an *ANC Lab Reporting Form*. |

#### After Treatment Discontinuation

<table>
<thead>
<tr>
<th>Previous Requirement</th>
<th>New Requirement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assess the patient’s ANC according to the monitoring frequency in the Prescribing Information. Document and submit the ANC results to the Clozapine REMS using the <em>Patient Status Form</em>.</td>
<td></td>
</tr>
</tbody>
</table>
More Information about the New Patient Status Form

This form must be completed monthly for each patient continuing treatment with clozapine. This form may also be used to:

- Interrupt, Discontinue, or Resume Treatment
- Designate the patient as a Benign Ethnic Neutropenia (BEN) patient
- Create a Treatment Rationale when the patient’s ANC level is < 1000/μL for a general population patient or < 500/μL for a BEN patient
- Designate the patient as a Hospice patient

The Patient Status Form may be completed by a certified prescriber or their designee. However, the following actions require the signature of a certified prescriber on the Patient Status Form:

- Designating a patient as a Hospice Care patient
- Designating a patient as a BEN patient
- Authorizing the continuation of therapy if one or more required labs are missing
- Creating a Treatment Rationale for a patient

A Patient Status Form must be received within 37 calendar days after the date of the Patient Enrollment Form or the last Patient Status Form.

If the Patient Status Form is not received within 37 calendar days, the patient is not authorized to receive clozapine until a completed form is received. If the Patient Status Form is missing, the pharmacist, if in possession of a current ANC within the acceptable range, may use a Dispense Rationale to dispense clozapine to the patient. A Dispense Rationale may be used up to three times per patient per year for outpatient dispensing.

The following questions are required to be answered on the Patient Status Form:

Are you monitoring the patient as recommended in the Prescribing Information? Yes/No

What is the patient’s current monitoring frequency? 3 times weekly, Weekly, Every 2 weeks, Monthly

Did the patient experience any adverse event(s) due to clozapine-induced neutropenia (e.g., infection)? Yes/No

The Patient Status Form may be submitted online or via a fax.

- To submit online, log into your account at www.clozapinerems.com and select the Manage Patient button. Select the Create or Add buttons for the appropriate patient.
- To submit via fax, complete the form and fax to 800-878-5927.
# How to Submit ANCs using the ANC Lab Reporting Form

ANCs may still be submitted via the *ANC Lab Reporting Form* online or via fax.

- To submit online, log into your account at www.clozapinerems.com and select the Manage Patient button. Select the Create or Add buttons in the Patient Status Form (PSF) column for the appropriate patient.
- To submit via fax, complete the ANC Lab Reporting Form and fax to 800-878-5927.

The Patient Status Form must still be submitted monthly.
Starting November 15, 2021, requirements to the Clozapine REMS will change.

**What are the important changes for pharmacies?**

<table>
<thead>
<tr>
<th>Obtaining Authorization to Dispense for Outpatient Pharmacies</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Previous Requirement</strong></td>
</tr>
<tr>
<td>Obtain a Predis pense Authorization (PDA) each time from the Clozapine REMS by accessing the Clozapine REMS website, Clozapine REMS Contact Center, or enabling the SWITCH (pharmacy management system) to support communication with the Clozapine REMS.</td>
</tr>
</tbody>
</table>

**RDAs may no longer be obtained via the SWITCH (the pharmacy management system).**

**A REMS Dispense Authorization (RDA) Verifies...**

- The patient is enrolled by a [certified prescriber or prescriber designee](#).
- A Patient Status Form has been completed by a certified [prescriber or prescriber designee](#) in the last 37 days.

For the first dispensing after patient enrollment, the RDA will verify that:

- the patient is enrolled
- the patient’s treatment is not interrupted or discontinued

For a subsequent dispensing, the RDA will verify that:

- the patient is enrolled
- a Patient Status Form has been completed in the last 37 days
- the prescriber has authorized the continuation of treatment if one or more labs are missing
- the prescriber has provided a Treatment Rationale if the most current ANC lab value is below the acceptable range
- the patient’s treatment is not interrupted or discontinued

If a Patient Status Form is not received, the pharmacist may use a Dispense Rationale to dispense (see Dispense Rationale below).
<table>
<thead>
<tr>
<th>Previous Requirement</th>
<th>New Requirement</th>
</tr>
</thead>
<tbody>
<tr>
<td>To avoid disruption in patient care, and to allow certified outpatient pharmacies an opportunity to apply clinical judgment to continue to dispense clozapine to enrolled patients, certified outpatient pharmacies will be allowed to provide a “Dispense Rationale” when a patient’s prescriber is not certified in the Clozapine REMS.</td>
<td>To avoid disruption in patient care, and to allow certified outpatient and inpatient pharmacies an opportunity to apply clinical judgment to continue to dispense clozapine to enrolled patients, certified pharmacies will be allowed to provide a “Dispense Rationale” when a Patient Status Form is not received from the patient’s prescriber within 37 days of the patient’s enrollment or previous Patient Status Form.</td>
</tr>
<tr>
<td>The Dispense Rationale will be automatically presented to the pharmacist when the RDA is rejected for this reason.</td>
<td>Three Dispense Rationales may be used per patient per year by outpatient pharmacies.</td>
</tr>
</tbody>
</table>
| To provide a Dispense Rationale, the pharmacist must be in possession of:  
- A current ANC (within 30 days of the attempted fill) within an acceptable range for the patient  
- The prescriber’s NPI number | There is no limit to the number of Dispense Rationales used by inpatient pharmacies. |

### Information about the New Patient Status Form

This form must be completed monthly by a certified prescriber or their designee for each patient continuing treatment with clozapine.

This form may also be used to:
- Interrupt, Discontinue, or Resume Treatment
- Designate the patient as a Benign Ethnic Neutropenia (BEN) patient
- Create a Treatment Rationale when the patient’s ANC level is < 1000/µL for a general population patient or < 500/µL for a BEN patient
- Designate the patient as a Hospice patient

A Patient Status Form must be received within 37 calendar days after the date of the Patient Enrollment Form or the last Patient Status Form.

The certified prescriber or their designee must provide the ANCs according to the patient’s current monitoring frequency. If an ANC is missing, the prescriber is required to provide authorization to continue therapy.

Continued on next page
Information about the New Patient Status Form (continued)

The *Patient Status Form* may also be used to create a Treatment Rationale to indicate that the benefits of continuing clozapine treatment outweigh the risk of neutropenia when the patient has moderate neutropenia (ANC 500-999/μL for the general population) or severe neutropenia (ANC < 500/μL for general population and patients with BEN).

How to Submit ANC*s* using the ANC Lab Reporting Form

ANCs may still be submitted via the *ANC Lab Reporting Form* online or via fax.

- To submit online, log into your account at www.clozapinerems.com and select the Submit ANC Lab button. Enter information to find the patient and then select the Continue button. Enter the ANC Lab information and select the Save button.
- To submit via fax, complete the ANC Lab Reporting Form and fax to 800-878-5927.

The Patient Status Form must still be submitted monthly.

<table>
<thead>
<tr>
<th>Certification Requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Previous Requirement</strong></td>
</tr>
<tr>
<td>----------------------------</td>
</tr>
<tr>
<td>Pharmacies must re-certify every two years.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Staff Training</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Previous Requirement</strong></td>
</tr>
<tr>
<td>Pharmacy staff must complete the Knowledge Assessment.</td>
</tr>
</tbody>
</table>
New Clozapine REMS Coming Nov 15th

- ALL Prescribers and Pharmacies **must re-certify** to continue to prescribe or dispense clozapine.

- ALL Patients continuing on clozapine **must be re-enrolled** by a certified prescriber or prescriber designee.

- **Start recertification and re-enrollment on August 16, 2021 to avoid interruption in patient treatment.**

Go to www.newclozapinerems.com

  - Click on Log-in | Register tab. You need to create new login credentials before re-certifying by clicking on Register.
New Clozapine REMS Requirements

- ALL Prescribers and Pharmacies **must re-certify** to continue to prescribe or dispense clozapine.
- ALL Patients continuing on clozapine **must be re-enrolled** by a certified prescriber or prescriber designee.
- Click on Log-in | Register tab. You need to create new login credentials before re-certifying by clicking on Register.
Important Program Update – current website

**UPDATE: New Clozapine REMS Coming November 15, 2021**


- **ALL Prescribers and Pharmacies must re-certificate** to continue to prescribe or dispense clozapine.
- **ALL Patients continuing on clozapine must be re-enrolled** by a certified prescriber or prescriber designee.

- **Start re-certification and re-enrollment on August 16, 2021 to avoid interruption in patient treatment**

  Go to www.newclozapinerems.com
  - Click on Log-in | Register tab. You need to create new login credentials before re-certifying by clicking on Register.
### Public Pages (pages accessible without logging into the website)
- Clozapine REMS Website Home page
- Contact Us page
- Find a Retail Pharmacy page (select Find, then select Find Retail Pharmacies)
- Find a Specialty Pharmacy page (select Find, then select Find Specialty Pharmacies)
- Wholesaler Verify Shipping Address – allows a wholesaler to verify that a pharmacy is certified (select Wholesaler)
- Wholesaler Verify Shipping Address – with Wholesaler’s DEA # verified (wholesaler is enrolled)
- Wholesaler Verify Shipping Address – with matching pharmacy destination selected
- Wholesaler Verify Shipping Address – with receipt generated (wholesaler is authorized to ship)
- Prescriber Public page
- Pharmacy Public page
- Patient Public page
- Patient Public page – with “What is a REMS?” selected and presented
- Patient Public page – with “What is the most serious risk of clozapine treatment?” selected and presented
- Patient Public page – with “What are the symptoms of infection?” selected and presented
- Patient Public page – with “What are the blood testing requirements for clozapine?” selected and presented
- Site Is Under Maintenance page (will be presented when the website is undergoing maintenance)
- Frequently Asked Questions

### User Authorization Screens
- Create Account – Pharmacy Authorized Representative (select Login | Register, then selected Register)
- Create Account – Prescriber (select Login | Register, then selected Register)
- Create Account – Choose Verification Method (to receive a verification code to verify the user’s identity)
- Create Account – Enter Verification Code
- Create Account – Complete
- Login/Register
- Reset Password
- Reset Password – Choose verification method (to receive a verification code to verify the user’s identity)
- Reset Password – Verification Code
- Reset Password – Completed
- My Account Preferences
- Change Account Information – Change Password
- Change Account Information – Password Change Completed
- Change Account Information – Verify identity via email
- Change Account Information – Verify identity via phone
- Change Account Information – Enter Code when verifying identity via email
Change Account Information – Enter Code when verifying identity via phone

Configure Authenticator App

Logged Out

Private Prescriber Pages (prescriber is logged into the website)

Private Prescriber Landing page – Prescriber Certified
Private Prescriber Landing page – Knowledge Assessment Pending, Enrollment Pending
Private Prescriber Landing page – Enrollment Complete, Knowledge Assessment Pending
Private Prescriber Landing page – Knowledge Assessment Complete, Enrollment Pending
Prescriber Knowledge Assessment page (not started)
Prescriber Knowledge Assessment page (unsuccessful attempt)
Prescriber Knowledge Assessment page (successful attempt)
Private Prescriber – Manage Patients page (available to both a certified prescriber and a prescriber designee)
Private Prescriber – ANC Lab Reporting Form (prescriber designee version with functionality limited for the designee)
Private Prescriber – ANC Lab Reporting Form (prescriber version with all functionality)
Private Prescriber – Patient Enrollment Form (prescriber designee version with functionality limited for the designee)
Private Prescriber – Patient Enrollment Form (prescriber version with all functionality)
Private Prescriber – Patient Status Form (prescriber designee version with functionality limited for the designee)
Private Prescriber – Patient Status Form (prescriber version with all functionality)
Private Prescriber – Patient Status Form (showing patient interrupted due to entry of an ANC indicating severe neutropenia)
Private Prescriber – ANC Calculator Modal Box from Monitoring Frequency
Private Prescriber – Prescriber editing his/her demographics
Private Prescriber – Prescriber Office Personnel Management (selected the Manage Designee button)
Private Prescriber – Adding a prescriber designee (choosing user type of online or phone only)
Private Prescriber – Adding a prescriber designee (phone only chosen)
Private Prescriber – Adding a prescriber designee (collecting demographics and sending invite)

Private Pharmacy Pages (pharmacy user is logged into the website)

Private Pharmacy Authorized Representative Landing page – Pharmacy Certified
Private Pharmacy Authorized Representative Landing page – Knowledge Assessment Pending, Enrollment Pending
Private Pharmacy Authorized Representative Landing page – Enrollment Complete, Knowledge Assessment Pending
Private Pharmacy Authorized Representative Landing page – Knowledge Assessment Complete, Enrollment Pending
Private Pharmacy Authorized Representative – Online Pharmacy Enrollment for Inpatient Pharmacy
Private Pharmacy Authorized Representative – Online Pharmacy Enrollment for Outpatient Pharmacy
Private Pharmacy Authorized Representative – Knowledge Assessment not started
Private Pharmacy Authorized Representative – Knowledge Assessment failed
Private Pharmacy Authorized Representative – Knowledge Assessment successful
Private Pharmacy Authorized Representative – Manage Personnel (only available to the authorized representative)
Private Outpatient Pharmacy Authorized Representative – Add Additional Staff page (Pharmacy Staff selected)

Private Outpatient Pharmacy Authorized Representative – Manage Pharmacies page (only available to the authorized representative)

Private Outpatient Pharmacy Authorized Representative – Add Additional Pharmacy page

Private Outpatient Pharmacy Authorized Representative – Submit ANC Lab Value, find a patient (selected the Submit ANC Lab button)

Private Outpatient Pharmacy Authorized Representative – Submit ANC Lab Value, patient found, showing monitoring activity

Private Outpatient Pharmacy – Obtain Patient RDA find the patient page - blank

Private Outpatient Pharmacy – Obtain Patient RDA find the patient page – no patient found error

Private Outpatient Pharmacy – Obtain Patient RDA find the patient page – too many patients found error

Private Outpatient Pharmacy – Obtain Patient RDA find the patient page – two patients found

Private Outpatient Pharmacy – Obtain Patient RDA find the patient page – two patients found, patient selected

Private Outpatient Pharmacy – Obtain Patient RDA, ready to obtain RDA

Private Outpatient Pharmacy – Obtain Patient RDA – RDA issued; safe use conditions collapsed

Private Outpatient Pharmacy – Obtain Patient RDA – RDA issued, safe use conditions expanded (initial prescription after enrollment), no dispensing information entered

Private Outpatient Pharmacy – Obtain Patient RDA – RDA issued, safe use conditions expanded (subsequent prescription with Patient Status Form), no dispensing information entered

Private Outpatient Pharmacy – Obtain Patient RDA – authorization rejected, safe use conditions expanded, Patient is discontinued

Private Outpatient Pharmacy – Obtain Patient RDA – authorization rejected, safe use conditions expanded, Patient treatment is interrupted

Private Outpatient Pharmacy – Obtain Patient RDA – authorization rejected, safe use conditions expanded, option for Dispense Rationale presented

Private Outpatient Pharmacy – Obtain Patient RDA – authorization rejected, safe use conditions collapsed, Patient has reached limit on Dispense Rationales

Private Outpatient Pharmacy – Obtain Patient RDA – RDA issued, dispensing information entered and saved

Private Outpatient Pharmacy – Obtain Patient RDA – RDA reversed
What is the Clozapine REMS?

The Clozapine REMS (Risk Evaluation and Mitigation Strategy) is a safety program required by the Food and Drug Administration (FDA) to manage the risk of severe neutropenia associated with clozapine treatment.

Severe neutropenia (absolute neutrophil count (ANC) less than 500/uL), can lead to serious and fatal infections.

---

To receive treatment, a patient must be enrolled in the Clozapine REMS by a certified doctor.

Pharmacies must be certified in the Clozapine REMS to receive and dispense clozapine.

If you are the designated authorized representative of a pharmacy, you can certify below.

Healthcare Providers must be certified in the Clozapine REMS to prescribe clozapine for outpatient use.

If you are a clozapine prescriber, you can certify below.

---

To report any SUSPECTED ADVERSE REACTIONS, contact the Clozapine REMS Contact Center at 1-888-586-0758 or FDA at 1-800-FDA-1088 or http://www.fda.gov/medwatch.
Contact the Clozapine REMS Contact Center

Phone
📞 1-888-586-0758

Fax
📠 1-800-878-5927

Hours of Operation

<table>
<thead>
<tr>
<th>Days</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>MONDAY - FRIDAY</td>
<td>8:00 AM - 8:00 PM ET</td>
</tr>
<tr>
<td>SATURDAY</td>
<td>8:00 AM - 4:30 PM ET</td>
</tr>
<tr>
<td>SUNDAY</td>
<td>Closed</td>
</tr>
</tbody>
</table>

Or

Contact a participating company about a specific product

### Branded Products

<table>
<thead>
<tr>
<th>Trade Name</th>
<th>Generic Name</th>
<th>Company</th>
<th>Links</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clozaril®</td>
<td>Clozapine</td>
<td>HLS Therapeutics (USA), Inc.</td>
<td>U.S. Prescribing Information and Medication Guide</td>
</tr>
<tr>
<td>Versacloz®</td>
<td>Clozapine, USP</td>
<td>Tasman Pharma Inc.</td>
<td>U.S. Prescribing Information and Medication Guide</td>
</tr>
</tbody>
</table>

### Generic Products

<table>
<thead>
<tr>
<th>Trade Name</th>
<th>Generic Name</th>
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<th>Links</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clozapine</td>
<td>Clozapine Tablets, USP</td>
<td>Accord Healthcare Inc.</td>
<td>U.S. Prescribing Information and Medication Guide</td>
</tr>
<tr>
<td>Clozapine</td>
<td>Clozapine Tablets, USP</td>
<td>Aurobindo Pharma USA Inc.</td>
<td>U.S. Prescribing Information and Medication Guide</td>
</tr>
<tr>
<td>Clozapine</td>
<td>Clozapine Tablets, USP</td>
<td>Mayne Pharma Inc.</td>
<td>U.S. Prescribing Information and Medication Guide</td>
</tr>
<tr>
<td>Clozapine</td>
<td>Clozapine Tablets, USP</td>
<td>Mayne Pharma Inc.</td>
<td>U.S. Prescribing Information and Medication Guide</td>
</tr>
<tr>
<td>Clozapine</td>
<td>Clozapine Tablets, USP</td>
<td>Mylan Pharmaceuticals Inc.</td>
<td>U.S. Prescribing Information and Medication Guide</td>
</tr>
<tr>
<td>Clozapine</td>
<td>Clozapine Tablets, USP</td>
<td>Mylan Pharmaceuticals Inc.</td>
<td>U.S. Prescribing Information and Medication Guide</td>
</tr>
<tr>
<td>Clozapine</td>
<td>Clozapine Tablets, USP</td>
<td>Mylan Pharmaceuticals Inc.</td>
<td>U.S. Prescribing Information and Medication Guide</td>
</tr>
<tr>
<td>Clozapine</td>
<td>Clozapine Tablets, USP</td>
<td>Sun Pharmaceutical Industries Inc.</td>
<td>U.S. Prescribing Information and Medication Guide</td>
</tr>
<tr>
<td>Clozapine</td>
<td>Clozapine, ODT</td>
<td>Teva Pharmaceuticals USA Inc.</td>
<td>U.S. Prescribing Information and Medication Guide</td>
</tr>
<tr>
<td>Clozapine</td>
<td>Clozapine Tablets, USP</td>
<td>Teva Pharmaceuticals USA Inc.</td>
<td>U.S. Prescribing Information and Medication Guide</td>
</tr>
</tbody>
</table>

To report any SUSPECTED ADVERSE REACTIONS, contact the Clozapine REMS Contact Center at 1-888-586-0758 or FDA at 800-FDA-1088 or http://www.fda.gov/medwatch.
Find Specialty Pharmacies
Specialty pharmacies certified to dispense clozapine.

**OutPat Test Pharmacy**
538 Deanna Forks
Filibertobury, VA 10726-7773

**XM Test Sub01 Pharmacy**
815 Daisy Gate
West Palls, ME 40254-1274

**XM Test Pharmacy**
358 Gorgia Forks
Fibury, MA 10726-7773

**OutPat Test Sub01 Pharmacy**
815 Enos Lock
East Dannie, DE 40254-1274

To report any SUSPECTED ADVERSE REACTIONS, contact the Clozapine REMS Contact Center at 1-888-586-0758 or FDA at 1-800-FDA-1088 or http://www.fda.gov/medwatch.
Verify Shipping Address

Generate receipts for proof of shipping destination verification

To get started, please verify your DEA number.

**Wholesaler DEA**

Your wholesaler's DEA Number 

[Verify]

Next, enter any combination of the following information and select the Find button.

**Destination NPI**

NPI Number

**Destination Name**

Search Healthcare Settings or Pharmacy...

**Destination Address**

Destination Address

**Destination City**

Destination City

**Destination State**

State

**Destination Postal Code**

5 digit Postal Code

[Clear] [Find]

If you cannot find the shipping destination, refine your search criteria and try again. Alternatively, contact the Clozapine REMS Contact Center 1-888-586-0758.
Verify Shipping Address

Generate receipts for proof of shipping destination verification

To get started, please verify your DEA number.

Wholesaler DEA
BN5623740
Verify

Next, enter any combination of the following information and select the Find button.

Destination NPI
NPI Number

Destination Name
Search Healthcare Settings or Pharmacy...

Destination Address
Destination City

Destination State
State

Destination Postal Code
5 digit Postal Code

If you cannot find the shipping destination, refine your search criteria and try again. Alternatively, contact the Clozapine REMS Contact Center 1-888-586-0758.
Verify Shipping Address

Generate receipts for proof of shipping destination verification

To get started, please verify your DEA number.

Wholesaler DEA

BN5623740

Verify

Next, enter any combination of the following information and select the Find button.

Destination NPI

NPI Number

OutPat Test Pharmacy

Destination Address

Destination City

Destination State

State

5 digit Postal Code

Destination Postal Code

Match Found

2110000000, OutPat Test Pharmacy, 538 Deanna Forks, Filiertobury, VA 10726-7773

Generate Receipt

If you cannot find the shipping destination, refine your search criteria and try again. Alternatively, contact the Clozapine REMS Contact Center 1-888-586-0758.
Shipping Verification Receipt

Store this receipt with your shipping records.

Destination:
OutPat Test Pharmacy
538 Deanna Forks
Filibertobury, VA 10726-7773

UTC Date and Time:
4/12/2021 8:54 PM

94fa1706-9798-4512-a368-a7f09956164e

Print

If you cannot find the shipping destination, refine your search criteria and try again. Alternatively, contact the Clozapine REMS Contact Center 1-888-586-0758.
To certify as a prescriber:

1. Review the Prescribing Information
   Review each drug's Prescribing Information
   - Clozaril®
   - Versacloz®
   - Clozapine Tablets, USP (Aurobindo Pharma USA)
   - Clozapine Tablets, USP (Aurobindo Pharma USA)
   - Clozapine Tablets, USP (Aurobindo Pharma USA)
   - Clozapine Tablets, USP (Mayne Pharma)
   - Clozapine Tablets, USP (Mayne Pharma)
   - Clozapine Tablets, USP (Mylan Pharmaceuticals)
   - Clozapine ODT (Mylan Pharmaceuticals)
   - Clozapine Tablets, USP (Mylan Pharmaceuticals)
   - Clozapine Tablets, USP (Sun Pharmaceutical Industries)
   - Clozapine Tablets, USP (Teva Pharmaceuticals USA)
   - Clozapine Tablets, USP (Teva Pharmaceuticals USA)
   - Clozapine Tablets, USP (Teva Pharmaceuticals USA)

2. Review the Guide for Healthcare Providers

3. Complete the Knowledge Assessment for Prescribers
   Successfully complete the Knowledge Assessment for Prescribers and submit it to the Clozapine REMS.
   □ Online or □ Print

4. Complete the Prescriber Enrollment Form
   Enroll in the Clozapine REMS by completing the Prescriber Enrollment Form and submitting it to the Clozapine REMS.
   □ Online or □ Print
Pharmacies must be certified in the Clozapine REMS to receive and dispense.

To certify your pharmacy:

1. Designate an Authorized Representative
   Designate an authorized representative to carry out the certification process and oversee implementation and compliance with the Clozapine REMS on behalf of the pharmacy.

2. Review the Pharmacy Information
   Have the authorized representative review the Clozapine and the Risk of Neutropenia: A Guide for Pharmacists.

3. Complete the Knowledge Assessment for Pharmacies
   Have the authorized representative successfully complete the Knowledge Assessment for Pharmacy and submit it to the Clozapine REMS.

4. Establish Processes and Procedures
   Establish processes and procedures to verify an available, current ANC is within the acceptable range for patients enrolled but not authorized to receive the drug.

5. Enroll Pharmacy
   Have the authorized representative enroll in the Clozapine REMS by completing the Pharmacy Enrollment Form and submitting it to the Clozapine REMS.

6. Train All Relevant Staff
   Train all relevant staff involved in dispensing clozapine on the requirements of the REMS program using the Clozapine and the Risk of Neutropenia: A Guide for Pharmacists.
Patient Enrollment

1. Talk With Your Clozapine Doctor
   Review A Guide for Patients and Caregivers: What You Need to Know about Clozapine and Neutropenia with your doctor.

2. Ask Questions!
   Make sure you understand what you need to do to take part in the Clozapine REMS.

3. Get Your Blood Test
   Get your blood tested as directed by your doctor. You must get your blood tested before you can receive clozapine from your pharmacy.

4. Pick Up Your clozapine Prescription
   Pick up your clozapine prescription from a pharmacy that is part of the Clozapine REMS. Your doctor will help you find a pharmacy that participates in the Clozapine REMS.

5. Tell Your Doctor Right Away
   Tell your doctor right away if you suffer any of the following symptoms while taking clozapine.
   - Infection, including skin, throat, urinary tract, vaginal, pneumonia, or any other infection
   - Fever or chills
   - Sores or ulcers inside your mouth, gums, or on your skin
   - Wounds that take a long time to heal
   - Feel like you have the flu
   - Pain or burning while urinating
   - Unusual vaginal discharge or itching
   - Abdominal pain
   - Sores or pain in or around your rectal area
   - Feel extremely weak or tired

To report any SUSPECTED ADVERSE REACTIONS, contact the Clozapine REMS Contact Center at 1-888-586-0758 or FDA at 1-800-FDA-1088 or http://www.fda.gov/medwatch.
What is a REMS?

A REMS is a drug safety program that the US Food and Drug Administration (FDA) can require for certain medicines with serious safety concerns. Drug companies and prescribers must take extra steps to make sure the benefits of using the drug are more than the risks. Clozapine has a REMS because of the risk of having a blood condition (severe neutropenia) that can lead to serious infections and death.

How to say REMS in English

- What is a REMS?
- What is the most serious risk of clozapine treatment?
- What are the symptoms of infection?
- What are the blood testing requirements for clozapine?
What is the most serious risk of clozapine treatment?

Clozapine can cause a blood condition (severe neutropenia), which can lead to serious infections and death. Neutropenia occurs when you have too few of a certain type of white blood cells called neutrophils. This makes it harder for your body to fight infections.

Before you can start clozapine and during treatment, you must have regular blood tests to measure the number of neutrophils you have in your blood. This test is called absolute neutrophil count (ANC). If the number of neutrophils, or ANC, is too low, you may have to stop clozapine. Your doctor will decide if or when it is safe to restart clozapine.

This is not the only serious risk associated with clozapine treatment. Talk to your doctor about the other serious risks.

How do you say Neutropenia?
What are the symptoms of infection?

⚠️ If you have any of these symptoms, talk to your doctor right away

- Infection, including skin, throat, urinary tract, vaginal, pneumonia, or any other infection
- Fever or chills
- Sores or ulcers inside your mouth, gums, or on your skin
- Wounds that take a long time to heal
- Feel like you have the flu
- Pain or burning while urinating
- Unusual vaginal discharge or itching
- Abdominal pain
- Sores or pain in or around your rectal area
- Feel extremely weak or tired

To report any SUSPECTED ADVERSE REACTIONS, contact the Clozapine REMS Contact Center at 1-888-586-0758 or FDA at 1-800-FDA-1088 or http://www.fda.gov/medwatch.
What are the blood testing requirements for clozapine?

- Your doctor will give you an order to have blood tests done.
- You will need to get your blood tested on the following schedule or as directed by your doctor:
  - Weekly blood tests for the first 6 months you are taking clozapine
  - Every 2 weeks for the next 6 months if your ANC stays normal
  - Monthly after the first year if your ANC stays normal

Results

- If your ANC is too low, your doctor will schedule blood tests more frequently.

Stay on clozapine

- The Clozapine REMS will keep track of your blood test results, so your doctor and pharmacist know if it is safe to fill your clozapine prescription.

Tell Your Doctor Right Away

Tell your doctor right away if you suffer any of the following symptoms while taking clozapine.
- Infection, including skin, throat, urinary tract, vaginal, pneumonia, or any other infection
- Fever or chills
- Sores or ulcers inside your mouth, gums, or on your skin
- Wounds that take a long time to heal
- Feel like you have the flu
- Pain or burning while urinating
- Unusual vaginal discharge or itching
- Abdominal pain
- Sores or pain in or around your rectal area
- Feel extremely weak or tired
SITE IS UNDER MAINTENANCE

Please check back soon.

Why is the site down?

The site is under maintenance because we are working on improving it.

What is the expected downtime?

We are usually back within 10-15 minutes, but it depends on the issue.

Do you need support?

You may call us at 1-888-586-0758 if you need support.
Create Account
Prescriber

Username and Password
Individual National Provider ID (NPI) Number

1000000050

☑️ I am
If the name above is incorrect, please re-enter your NPI number.

Password

**************

Confirm Password

**************

Cancel
Next
Create Account
Verify Identity

Choose verification method

We will send you a code to verify your identity. The code may only be used once and is time sensitive.

● Email me the code

verifytest74839@examoto.net

After logging in, use preferences to add password reset options and/or enable multi-factor authentication.

Cancel  Next
Create Account
Verify Identity

Enter Verification Code
Please enter your code.

472795

Cancel  Next
Create Account
Complete

RxAuthRep333@examoto.net, your account has been created.
You may now login to perform REMS functions online.

Login
Login

Username (click i for additional help)

Password

☐ Remember my login

Forgot your password?

Login

Register

To perform REMS functions online, you must have an account. Creating an account involves creating unique login credentials (username and password). Register to create an account.

Or

Register

To report any SUSPECTED ADVERSE REACTIONS, contact Clozapine REMS Contact Center at 1-888-586-0758 or FDA at 800-FDA-1088 or http://www.fda.gov/medwatch.
Reset Password

Username

[User ID | NPI number]

Cancel  Next
Reset Password

Verify Identity

Choose verification method

We will send you a code to verify your identity. The code may only be used once and is time sensitive.

○ Email Txxxxxxxxxxx@EXAMOTO.NET
○ Text (SMS) xxx-xxx-8306
○ Call xxx-xxx-8306
○ Approve request on my Authenticator App

After logging in, use preferences to add password reset options and/or enable multi-factor authentication.

Cancel  Next
Reset Password

Verify Code

We sent you a code to verify your identity; please enter it here.

Code

543509

Password

**********

Confirm password

**********

Cancel  Next
Reset Password
Completed

Your password has been reset.

Continue
My Account
Preferences

Identity
- Username: 1310000000
  You may only change your username by calling the coordinating center at 1-888-586-0758.
- Password:
- First/Last Name: PRJane PRDoe
  Change my First/Last Name

Verification Methods
- Email: testr26056@examoto.net
  Change my Email
- Phone: 610-243-2826
  Change my Phone Number
- Authenticator App: Configured
  Reset my App

Two-Factor Authentication
Two-factor authentication (2FA) improves security. 2FA adds a second level of authentication to an account login. With 2FA enabled, the user is required to enter their username, password and a code. The code can be provided via several methods.

Use Two-Factor Authentication to improve security
- Two-Factor Authentication: Disabled
  Enable
Change Account Information
Completed

Your password has been changed.

Continue
Change Account Information
Email Address

We will send you a code to verify your identity. The code may only be used once and is time sensitive.

✉️ Enter Email
Email

[ ] Cancel [ ] Next

To report any SUSPECTED ADVERSE REACTIONS, contact Clozapine REMS Contact Center at 1-888-586-0758 or FDA at 800-FDA-1088 or http://www.fda.gov/medwatch.
Change Account Information
Phone Number

We will send you a code to verify your identity. The code may only be used once and is time sensitive.

Phone
nnnn-nnnn-nnnn

○ Text (SMS) me with the code ○ Call me with the code

Cancel    Next
Change Account Information

Verify Email Address

We sent you a code to verify your identity; please enter it here.

Code

440553

I didn't receive the code

Next
Change Account Information
Verify Phone Phone Number

We sent you a code to verify your identity; please enter it here.

Code

840655

I didn't receive the code  Next
Account Options
Configure Authenticator App

Follow these steps to use an authenticator app:

1. Download a two-factor authenticator app, like Microsoft Authenticator or Google Authenticator for Android or iOS.

2. Scan the QR Code or enter this key into your two-factor authenticator app:
   
   **NVLS C4GA MQWN EGPO RRH3 LLGU ILT5 TBZK**
   
   The spaces are not required, and the code is not case-sensitive.

3. Once you have scanned the QR code or input the key above, your two-factor authentication app will provide you with a unique code. Enter the code in the confirmation box below and select VERIFY.

   Code
   
   nnnnnn

   Cancel  Verify
Logged Out

You are now logged out.

Click [here](#) to return to the Clozapine REMS application.

To report any SUSPECTED ADVERSE REACTIONS, contact Clozapine REMS Contact Center at 1-888-586-0758 or FDA at 800-FDA-1088 or [http://www.fda.gov/medwatch](http://www.fda.gov/medwatch).
Prescriber Certification
You are currently certified in the Clozapine REMS.

Edit Personnel
Edit, Add, or Remove Designees from the Clozapine REMS

Enroll Patients in the Clozapine REMS
You must enroll your patients in the Clozapine REMS.

Manage Patients
Manage your Clozapine REMS patients.

Prescriber Materials

Knowledge Assessment for Prescribers
Prescriber Enrollment Form
Patient Enrollment Form
Patient Status Form
ANC Lab Reporting Form
Prescriber Designee Enrollment Form
What's Changed in the Clozapine REMS for Prescribers?

Upload Form
Uploads must be in PDF format.

Browse
Or drop files here
Prescriber Certification
You must certify in the Clozapine REMS to prescribe clozapine. To certify please complete the following:

1. Review the clozapine prescribing information:
   - Clozaril®
   - Versaclozar®
   - Clozapine Tablets, USP (Accord Healthcare)
   - Clozapine Tablets, USP (Aurobindo Pharma USA)
   - Clozapine Tablets, USP (Aurobindo Pharma USA)
   - Clozapine Tablets, USP (Mayne Pharma)
   - Clozapine Tablets, USP (Mayne Pharma)
   - Clozapine Tablets, USP (Mylan Pharmaceuticals)
   - Clozapine ODT (Mylan Pharmaceuticals)
   - Clozapine Tablets, USP (Mylan Pharmaceuticals)
   - Clozapine ODT (Mylan Pharmaceuticals)
   - Clozapine Tablets, USP (Sun Pharmaceutical Industries)
   - Clozapine Tablets, USP (Teva Pharmaceuticals USA)
   - Clozapine Tablets, USP (Teva Pharmaceuticals USA)
   - Clozapine Tablets, USP (Teva Pharmaceuticals USA)

2. Review the Guide for Healthcare Providers


   3. Complete the Knowledge Assessment for Prescribers

   Successfully complete the Knowledge Assessment for Prescribers and submit it to the Clozapine REMS.

   4. Complete the Prescriber Enrollment Form

   Enroll in the Clozapine REMS by completing the Prescriber Enrollment Form and submitting it to the Clozapine REMS.

Upload Form
Uploads must be in PDF format.

- [Browse]
- [Or drop files here]

Prescriber Office Personnel Management
Edit, Add, Remove Designees from the Clozapine REMS

- [Manage Designees]

Enroll Patients in the Clozapine REMS
You must enroll your patients in the Clozapine REMS.

- [Enroll Patient]

Manage Patients
Manage your Clozapine REMS patients.

- [Manage Patients]
<table>
<thead>
<tr>
<th>Name</th>
<th>Date of Birth</th>
<th>REMS Patient ID</th>
<th>Population</th>
<th>Monitoring</th>
<th>Treatment Status</th>
<th>Patient Status Form (PSF)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Pat Smith</td>
<td>06/27/1954</td>
<td>CPDemoPatDiscont</td>
<td>General</td>
<td>N/A</td>
<td>Discontinued</td>
<td>Add PSF</td>
</tr>
<tr>
<td>Patient Pat Smith</td>
<td>06/27/1954</td>
<td>CMDemoSoLate</td>
<td>General</td>
<td>3 times a week</td>
<td>Active</td>
<td>15 days Late</td>
</tr>
<tr>
<td>Patient Pat Smith</td>
<td>08/27/1954</td>
<td>CMDemoWeekly</td>
<td>General</td>
<td>Weekly</td>
<td>Active</td>
<td>Add PSF</td>
</tr>
<tr>
<td>Patient Pat Smith</td>
<td>06/27/1954</td>
<td>CMDemoIn01</td>
<td>General</td>
<td>3 times a week</td>
<td>Interrupted</td>
<td>Add PSF</td>
</tr>
<tr>
<td>Patient Terry Smith</td>
<td>09/22/1989</td>
<td>CMDemoEv2Wk</td>
<td>General</td>
<td>Every 2 weeks</td>
<td>Active</td>
<td>Add PSF</td>
</tr>
<tr>
<td>Patient Pat Smith</td>
<td>06/27/1954</td>
<td>CMDemoMonthly</td>
<td>General</td>
<td>Monthly</td>
<td>Active</td>
<td>Due in 3 days</td>
</tr>
<tr>
<td>Patient Pat Smith</td>
<td>07/15/1965</td>
<td>CPatEg300K07</td>
<td>General</td>
<td>Weekly</td>
<td>Active</td>
<td>6 days Late</td>
</tr>
<tr>
<td>Patient Pat Smith</td>
<td>07/15/1965</td>
<td>CMDemoBenMonthly</td>
<td>BEN</td>
<td>Monthly</td>
<td>Active</td>
<td>Add PSF</td>
</tr>
<tr>
<td>Patient Julie Williams</td>
<td>06/13/1970</td>
<td>PA1294567</td>
<td>General</td>
<td>Weekly</td>
<td>Unknown</td>
<td>Add PSF</td>
</tr>
<tr>
<td>Patient Jenn Miller</td>
<td>10/31/1988</td>
<td>PA7654321</td>
<td>General</td>
<td>Weekly</td>
<td>Unknown</td>
<td>Add PSF</td>
</tr>
</tbody>
</table>

Edit patient demographics

Showing 1 to 10 of 21 entries
ANC Lab Reporting Form

Patient ANC Monitoring

This form may be used by certified prescribers and their designees to submit an ANC Lab outside of the monthly reporting requirement (using the Patient Status Form).

Note: Report of an ANC lab value indicating moderate (general population) or severe neutropenia (general or BBN population) requires treatment to be interrupted or discontinued or the creation of a Treatment Rationale by the prescriber unless a more recent ANC lab value is provided that is ≥ 1500/L for a general population patient or ≥ 500/L for a BBN population patient.

Enrolled as of 2/26/2021

Name: Patient Pat Smith
Date of Birth: 6/27/1954
REMS Patient ID: CMDemo3x3late
Zip Code: 52722
Phone: 920-723-6334
Email: CMPatients@email.net

Monitoring History

Search:

Date 02/26/2021
Monitoring Frequency - 3 times a week

ANC Entry

Current Patient Monitoring Frequency: 3 times a week

Blood Draw Date

MM/DD/YYYY

Reason for Missing Lab

- Patient Refused
- Clinician Discretion
- Extraline factors (e.g., weather, transportation issues)

General Patient Population

- Normal Range (≥ 1500/L)
- Mild Neutropenia (1000 to 1499/L)
- Moderate Neutropenia (500 to 999/L)
- Severe Neutropenia (< 500/L)

ANC (per L)

Cancel    Save
ANC Lab Reporting Form

Patient ANC Monitoring
This form may be used by certified prescribers and their designees to submit an ANC Lab outside of the monthly reporting requirement (using the Patient Status Form).

Patient (Population: General)  Enrolled as of 2/26/2021

Name: PatientPat Smith  Phone: 
Date of Birth: 6/27/1954  Email: CMPatient@examoto.net
RXMS Patient ID: CMDemoWeekly  Zip Code: 52722

Monitoring History

Search:

Date  Monitoring Activity
03/28/2021  Monitoring Frequency - Weekly
03/29/2021  ANC Lab Value - Normal Range (≥ 1500/μL)
04/05/2021  ANC Lab Value - Normal Range (≥ 1500/μL)

ANC Entry

Current Patient Monitoring Frequency: Weekly

Blood Draw Date: MM/DD/YYYY

Reason for Missing Lab:
- Patient Refused
- Clinician Discretion
- Extrinsic factors (e.g., weather, transportation issues)

General Patient Population

ANC (per μL)
- Normal Range (≥ 1500/μL)
- Mild Neutropenia (1000 to 1499/μL)
- Moderate Neutropenia (500 to 999/μL)
- Severe Neutropenia (< 500/μL)

Cancel  Save
Patient Enrollment

Note: Only a certified prescriber may enroll a Benign Ethnic Neutropenia (BEN) patient or a hospice patient. Sections of this form requiring input may only be completed by a Certified Prescriber.

**Patient Enrollment**

**First Name** | **Last Name**
--- | ---
First Name | Last Name

**Gender**
- Male
- Female
- Other

**Date of Birth**

**Race**
- American Indian or Alaska Native
- Asian
- Black or African American
- Caucasian
- Native Hawaiian or Other Pacific Islander
- Other

**Ethnicity**
- Hispanic or Latino
- Not Hispanic or Latino

**Phone**

**Email**

**Does the patient have a permanent address?**

**Zip Code**

**Patient Information**

Is this patient actively on clozapine therapy?
- Yes
- No
- Unknown

If Yes, what is this patient’s current monitoring frequency?

**Monitoring**

**Frequency**

**Baseline Lab Information**

**Blood Draw Data** | **ANC (per μL)**
--- | ---

**Baseline Ethnic Neutropenia (BEN) Patient Attestation**

Complete this section to indicate that this is a patient with documented baseline ethnic neutropenia.

- A BEN patient designation provides a separate ANC monitoring algorithm for the patient.
- The BEN designation is a permanent status.

**Hospital Care Patient Attestation**

For hospice patients (i.e., terminally ill patients with an estimated life expectancy of six months or less), the prescriber may reduce the ANC monitoring frequency to once every 6 months after a discussion with the patient and his/her caregivers.

- This is a hospice care patient

[Cancel] | [Enroll Patient]
Patient Enrollment

First Name  Lunch Name

Gender  Date of Birth

☐ Male  ☐ Female  ☐ Other

Race

☐ American Indian or Alaska Native  ☐ Asian  ☐ Black or African American  ☐ Caucasian  ☐ Native Hawaiian or Other Pacific Islander  ☐ Other

Ethnicity

☐ Hispanic or Latino  ☐ Not Hispanic or Latino

Phone  Email

☐ Does the patient have a permanent address?  Zip Code

Patient Information

Is this patient actively on clozapine therapy?

☐ Yes  ☐ No  ☐ Unknown

If Yes, what is this patient’s current monitoring frequency?

☐ Monitoring

Frequency

☐ Daily  ☐ Weekly  ☐ Monthly

Baseline Lab Information

Blood Draw Date  ANC (per L)

MM/DD/YYYY  0

Benign Ethnic Neutropenia (BEN) Patient Attestation

☐ Benign Ethnic Neutropenia (BEN)

Complete this section to indicate that this is a patient with documented benign ethnic neutropenia.

☐ A BEN patient designation provides a separate ANC monitoring algorithm for the patient. The BEN designation is a permanent status.

Hospice Care Patient Attestation

☐ Hospice Care

For hospice patients (i.e., terminally ill patients with an estimated life expectancy of six months or less), the prescriber may reduce the ANC monitoring frequency to once every 6 months after a discussion with the patient and their caregiver.

☐ This is a hospice care patient

Cancel  Enroll Patient
### Patient Status Form (PSF)

**Patient (Dependent or General)**

<table>
<thead>
<tr>
<th>Name: Patient Troy Smith</th>
<th>Zip Code: 28841</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of Birth: 9/22/1969</td>
<td>Phone: 920-720-6529</td>
</tr>
<tr>
<td>REMS Patient ID: CMWmedic3@Wks</td>
<td>Email: <a href="mailto:CMIrsmith@exomeric.net">CMIrsmith@exomeric.net</a></td>
</tr>
</tbody>
</table>

**Patient Status**

- **Are you monitoring the patient as recommended in the Prescribing Information?** [ ] Yes  [ ] No

**Monitoring**

- **Current Patient Monitoring Frequency:** Every 2 weeks
- **Change the patient’s monitoring frequency to:** [ ] Daily [ ] Weekly

**Hospice Care**

- For hospice patients or terminal illness patients with an estimated life expectancy of 6 months or less, the prescriber may reduce the ANC monitoring frequency to once every 6 months after a discussion with the patient and the prescriber’s completer.

**Did the patient experience any adverse event(s) due to clozapine-induced neutropenia (e.g., infection)?**

- [ ] Yes  [ ] No

**Patient Treatment Status Update**

- [ ] Discontinue Treatment
- [ ] Reduce Treatment

**Severe Ethic Neutropenia (SIN)**

- Complete this section to indicate that this is a patient with documented severe ethic neutropenia.

- A SIN patient designation provides a separate ANC monitoring algorithm for the patient. The SIN designation is permanent status.

### Reporting ANC Lab Data

#### Blood Draw Date

<table>
<thead>
<tr>
<th>MM/DD/YYYY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reason for Missing Lab</td>
</tr>
<tr>
<td>[ ] Patient-Related</td>
</tr>
<tr>
<td>[ ] Clinician Decision</td>
</tr>
<tr>
<td>[ ] Extraneous factors (e.g., weather, transportation issues)</td>
</tr>
</tbody>
</table>

#### General Patient Population

<table>
<thead>
<tr>
<th>Normal Range: 5.500-10.000/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANC (per µL)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Normal Range: 1.500-4.500/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANC (per µL)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Normal Range: 1.000-2.999/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANC (per µL)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Normal Range: 0.500-0.999/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANC (per µL)</td>
</tr>
</tbody>
</table>

### Add Supplemental ANC

#### Blood Draw Date

<table>
<thead>
<tr>
<th>MM/DD/YYYY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reason for Missing Lab</td>
</tr>
<tr>
<td>[ ] Patient-Related</td>
</tr>
<tr>
<td>[ ] Clinician Decision</td>
</tr>
<tr>
<td>[ ] Extraneous factors (e.g., weather, transportation issues)</td>
</tr>
</tbody>
</table>

#### General Patient Population

<table>
<thead>
<tr>
<th>Normal Range: 5.500-10.000/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANC (per µL)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Normal Range: 1.500-4.500/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANC (per µL)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Normal Range: 1.000-2.999/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANC (per µL)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Normal Range: 0.500-0.999/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANC (per µL)</td>
</tr>
</tbody>
</table>

### Cancel  Save
Access the patient by obtaining complete blood counts, including the absolute neutrophil count (ANC) as described in the Prescribing Information.

This form must be completed monthly for each patient continuing treatment with clozapine.

**Patient Information**

<table>
<thead>
<tr>
<th>Field</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name</td>
<td></td>
</tr>
<tr>
<td>Date of Birth</td>
<td></td>
</tr>
<tr>
<td>REMS Patient ID</td>
<td></td>
</tr>
<tr>
<td>Zip Code</td>
<td></td>
</tr>
<tr>
<td>Phone</td>
<td></td>
</tr>
<tr>
<td>Email</td>
<td></td>
</tr>
</tbody>
</table>

**Patient Status**

Are you monitoring the patient as recommended in the Prescribing Information?

- [ ] Yes
- [ ] No

**Monitoring**

Current Patient Monitoring Frequency: [ ]

Are you changing the patient’s monitoring frequency to:

- [ ] [ ]
- [ ] [ ]

**Hospital Care**

For patients who have been treated with clozapine and have had an ANC of less than 500 μL or less, the frequency of monitoring the ANC may increase. The frequency of monitoring the ANC should not exceed every 6 months after a decision to discontinue the patient and his/her caregiver. I want to change this patient’s monitoring frequency to once every 6 months for a hospital patient.

- [ ] Yes
- [ ] No

**Did the patient experience any adverse event(s) due to clozapine-induced neutropenia (eg, infection)?**

- [ ] Yes
- [ ] No

**Patient Treatment Status Update**

Complete this section to interrupt, discontinue, or resume treatment for this patient.

- [ ] Interrupt Treatment
- [ ] Discontinue Treatment
- [ ] Resume Treatment

**Benign or Severe Neutropenia (BEN)**

Complete this section to indicate that this is a patient with documented benign or severe neutropenia.

- [ ] BEN: Patient is in remission
- [ ] BEN: Patient is in remission

**Reporting ANC Lab Data**

**Blood Draw Data**

<table>
<thead>
<tr>
<th>Reason for Missing Lab</th>
<th>ANC (per μL)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal Range (≥ 1500 μL)</td>
</tr>
<tr>
<td></td>
<td>Mild Neutropenia (1000–1499 μL)</td>
</tr>
<tr>
<td></td>
<td>Moderate Neutropenia (950–999 μL)</td>
</tr>
<tr>
<td></td>
<td>Severe Neutropenia (&lt; 950 μL)</td>
</tr>
</tbody>
</table>

**Blood Draw Date**

<table>
<thead>
<tr>
<th>ANC (per μL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Range (≥ 1500 μL)</td>
</tr>
<tr>
<td>Mild Neutropenia (1000–1499 μL)</td>
</tr>
<tr>
<td>Moderate Neutropenia (950–999 μL)</td>
</tr>
<tr>
<td>Severe Neutropenia (&lt; 950 μL)</td>
</tr>
</tbody>
</table>

**Patient Treatment Status**

Due to the last ANC value entered indicating either the patient has moderate neutropenia (ANC 950–999 μL) or severe neutropenia (ANC < 950 μL), for general population with PCP, the treatment status has been set to interruption. You may choose to discontinue treatment or provide a treatment rationale below.

- [ ] Interrupt Treatment
- [ ] Treatment Rationale
- [ ] Benefits of continuing clozapine treatment outweigh the risk of neutropenia.
- [ ] Not to exceed 6 months
- [ ] Discontinue Treatment

Next
**ANC Calculator**

**ANC (per µL)**

**WBC count (x10⁹/mm³)**
- 0.0
- Segs
- 0%
- Neutrophils
- 0%
- Bands
- 0%

**ANC (per µL)**

**WBC count (x10⁹/mm³)**

- C
- =

**Note:**
For WBC count, data should be entered in decimal format (e.g. a value of 4.300 should be entered as 4.3).


**General Patient Population**
- Normal Range (≥ 1500/µL)
- Mild Neutropenia (1000 to 1499/µL)
- Moderate Neutropenia (500 to 999/µL)
- Severe Neutropenia (< 500/µL)

**ANC (per µL)**
### Prescriber

**PRJane PRDoe**

<table>
<thead>
<tr>
<th>Individual NPI Number</th>
<th>Individual DEA #</th>
</tr>
</thead>
<tbody>
<tr>
<td>1310000000</td>
<td>DEA Number</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>First Name</th>
<th>Middle Initial</th>
<th>Last Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRJane</td>
<td>Middle Initial</td>
<td>PRDoe</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinic/Practice Name</th>
<th>Address Line 1</th>
<th>Address Line 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test Prescriber Practice</td>
<td>12 Parker Avenue</td>
<td>Address Line 2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>City</th>
<th>State</th>
<th>Zip Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chambersburg</td>
<td>Pennsylvania</td>
<td>17201</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Number</th>
<th>Extension</th>
<th>Fax</th>
<th>Email</th>
</tr>
</thead>
<tbody>
<tr>
<td>426-689-9443</td>
<td>mnn...</td>
<td>209-772-9961</td>
<td><a href="mailto:PR13100000000@examoto.net">PR13100000000@examoto.net</a></td>
</tr>
</tbody>
</table>

In general, what is the best time to contact you?

- [ ] Morning
- [ ] Afternoon
- [x] Evening

Preferred Method of Contact

- [x] Email
- [ ] Text
- [ ] Call

[Cancel] [Save]
### Prescriber Office Personnel Management

**PRJane PRDoe**

- **Prescriber**
- **Enrolled: 19th July, 2014**

<table>
<thead>
<tr>
<th>Action</th>
<th>Role</th>
<th>Name</th>
<th>Email</th>
<th>Added</th>
<th>Days Inactive</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>PRJohn DesigneeSmith</td>
<td><a href="mailto:PRDesignee@Examoto.net">PRDesignee@Examoto.net</a></td>
<td>1/1/2021</td>
<td>102</td>
</tr>
</tbody>
</table>

Showing 1 to 1 of 1 entries
Additional Designees

How will this designee interact with the Clozapine REMS?

- Allow this designee to be authorized to perform functions on my behalf via the Clozapine REMS Contact Center only. This designee will not be able to perform functions on my behalf via the Clozapine REMS website.

- Allow this designee to create login credentials for the Clozapine REMS website. The designee will also be authorized to perform functions on my behalf via the Clozapine REMS Contact Center.

To report any SUSPECTED ADVERSE REACTIONS, contact the Clozapine REMS Contact Center at 1-800-586-0750 or FDA at 1-800-FDA-1098 or http://www.fda.gov/medwatch.
Prescriber Office Personnel Management

Additional Designees

How will this designee interact with the Clozapine REMS?

☐ Allow this designee to be authorized to perform functions on my behalf via the Clozapine REMS Contact Center only. This designee will not be able to perform functions on my behalf via the Clozapine REMS website.

☐ Allow this designee to create login credentials for the Clozapine REMS website. The designee will also be authorized to perform functions on my behalf via the Clozapine REMS Contact Center.

For a designee who will only interact via the Clozapine REMS Contact Center, please download and submit the Prescriber Designee Enrollment Form to the Clozapine REMS either via upload or fax to 1-800-878-5927.

Return
Pharmacy
Outpatient Pharmacy Group

To certify your pharmacy:
Your pharmacy is currently certified.

Obtain a Patient’s REMS Dispense Authorization (RDA)
An RDA is a receipt from the Clozapine REMS signifying that the REMS requirements to dispense for this patient are currently met.

Submit a Patient’s ANC Lab Value
Pharmacists in possession of a patient’s ANC lab value are encouraged to enter it into the Clozapine REMS. A submitted ANC lab will be visible to the patient's prescriber and pharmacy personnel attempting to obtain an RDA.

Pharmacy Personnel
A pharmacy can have multiple personnel with online accounts. You may invite personnel or remove them.

Pharmacies
A pharmacy can have multiple pharmacies grouped together under the responsibility of a Pharmacy Authorized Representative.

Pharmacy Materials
- Clozapine and the Risk of Neutropenia: A Guide for Pharmacists
- Knowledge Assessment for Pharmacies
- Inpatient Pharmacy Enrollment Form
- Outpatient Pharmacy Enrollment Form
- ANC Lab Reporting Form
- RDA Factsheet for Inpatient Pharmacies
- RDA Factsheet for Outpatient Pharmacies
- What’s Changed in the Clozapine REMS for Pharmacies?

Upload Form
Uploads must be in PDF format.

Browse
Or drop files here
To certify your pharmacy:
Your pharmacy must certify in the Clozapine REMS to dispense clozapine. To certify please complete the following:

1. Review the Pharmacy Information
   Have the authorized representative review the Clozapine and the Risk of Neutropenia: A Guide for Pharmacists.

2. Complete the Knowledge Assessment for Pharmacies
   Have the authorized representative successfully complete the Knowledge Assessment for Pharmacy and submit it to the Clozapine REMS.

3. Enroll Pharmacy
   
   ▶ Sign and Submit

Obtain a Patient’s REMS Dispense Authorization (RDA)
An RDA is a receipt from the Clozapine REMS signifying that the REMS requirements to dispense for this patient are currently met.

Submit a Patient’s ANC Lab Value
Pharmacists in possession of a patient’s ANC lab value are encouraged to enter it into the Clozapine REMS. A submitted ANC lab will be visible to the patient’s prescriber and pharmacy personnel attempting to obtain an RDA.

Pharmacy Personnel
A pharmacy can have multiple personnel with online accounts. You may invite personnel or remove them.

Pharmacies
A pharmacy can have multiple pharmacies grouped together under the responsibility of a Pharmacy Authorized Representative.
To certify your pharmacy:

1. Review the Pharmacy Information

Have the authorized representative review the Clozapine and the Risk of Neutropenia: A Guide for Pharmacists.

2. Complete the Knowledge Assessment for Pharmacies

Have the authorized representative successfully complete the Knowledge Assessment for Pharmacy and submit it to the Clozapine REMS.

Enroll Pharmacy

Have the authorized representative enroll in the Clozapine REMS by completing the Pharmacy Enrollment Form and submitting it to the Clozapine REMS.

Obtain a Patient’s REMS Dispense Authorization (RDA)

An RDA is a receipt from the Clozapine REMS signifying that the REMS requirements to dispense for this patient are currently met.

Submit a Patient’s ANC Lab Value

Pharmacists in possession of a patient’s ANC lab value are encouraged to enter it into the Clozapine REMS. A submitted ANC lab will be visible to the patient’s prescriber and pharmacy personnel attempting to obtain an RDA.

Pharmacy Personnel

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Pharmacies

A pharmacy can have multiple pharmacies grouped together under the responsibility of a Pharmacy Authorized Representative.
Pharmacy
Outpatient Pharmacy

To certify your pharmacy:
Your pharmacy must certify in the Clozapine REMS to dispense clozapine. To certify please complete the following:

1. Review the Pharmacy Information
   Have the authorized representative review the Clozapine and the Risk of Neutropenia: A Guide for Pharmacists.

2. Complete the Knowledge Assessment for Pharmacies
   Have the authorized representative successfully complete the Knowledge Assessment for Pharmacy and submit it to the Clozapine REMS.

3. Enroll Pharmacy
   → Sign and Submit

Obtain a Patient’s REMS Dispense Authorization (RDA)
An RDA is a receipt from the Clozapine REMS signifying that the REMS requirements to dispense for this patient are currently met.

→ Obtain Patient RDA

Submit a Patient’s ANC Lab Value
Pharmacists in possession of a patient’s ANC lab value are encouraged to enter it into the Clozapine REMS. A submitted ANC lab will be visible to the patient’s prescriber and pharmacy personnel attempting to obtain an RDA.

→ Submit ANC Lab

Pharmacy Personnel
A pharmacy can have multiple personnel with online accounts. You may invite personnel or remove them.

→ Manage Personnel

Pharmacies
A pharmacy can have multiple pharmacies grouped together under the responsibility of a Pharmacy Authorized Representative.

→ Manage Pharmacies

Pharmacy Materials

Clozapine and the Risk of Neutropenia: A Guide for Pharmacists
Knowledge Assessment for Pharmacies
Inpatient Pharmacy Enrollment Form
Outpatient Pharmacy Enrollment Form
ANC Lab Reporting Form
RDA Factsheet for Inpatient Pharmacies
RDA Factsheet for Outpatient Pharmacies
What’s Changed in the Clozapine REMS for Pharmacies?

Upload Form
Uploading must be in PDF format.

Browse
Or drop files here
Pharmacy Enrollment

The earliest timeframe for the pharmacy to:
1. Become a REMS Participant
2. Successfully complete the Knowledge Assessment for Pharmacists
3. Complete a submission to the Pharmacy in Training along with the optional Knowledge Assessment for Pharmacists
4. Implement the necessary staff training/educational processes to comply with the REMS requirements

Pharmacy Information:

Organizational NPI Number

[Select address type to prepopulate form]

Office Address

Pharmacy Name

[Pharmacy Name]

Address Line 1

Address Line 2

City

State

Zip Code

Number

Extension

Fax

DEA Number

DEA Number

Pharmacy Address Information:

Individual's Name

Last Name

Address

Position

Title

Extension

Fax

Phone Number

Fax

Preferred Method of Contact

Email

screen@pharmacy.com

Pharmacy Authorized Representative Responsibilities

Pharmacy Type (Pharmacies have different REMS requirements):

Retail Pharmacy

Institutional Pharmacy

By Authorized Representative, I attest to:

- Having obtained and read the Knowledge Assessment for Pharmacists and submit it to the Clozapine REMS.

- Ensuring all processes and procedures are verified, either through the acceptable range for patients enrolled but not authorized to receive Clozapine at the pharmacy, or by obtaining confirmations from an Authorized Representative.

- Ensuring that a written or electronic copy of the Knowledge Assessment for Pharmacists is submitted to Clozapine REMS.

Before the date, all pharmacy staff must:

- Confirm that all staff have completed this Knowledge Assessment for Pharmacists.

- Obtain a copy of the Knowledge Assessment for Pharmacists from the pharmacist.

- Verify that all staff have completed the Knowledge Assessment for Pharmacists.

At discharge, all pharmacy staff must:

- Ensure that a copy of the Knowledge Assessment for Pharmacists is completed by the patient.

- Provide a copy of the Knowledge Assessment for Pharmacists to the pharmacist.

To obtain certification of compliance, an authorized representative must:

- Submit the completed copy of the Knowledge Assessment for Pharmacists to Clozapine REMS.

- Submit the completed copy of the Knowledge Assessment for Pharmacists to the pharmacist.

- Submit the completed copy of the Knowledge Assessment for Pharmacists to Clozapine REMS.
Pharmacy Enrollment

The following representatives for the pharmacy must:
1. Review by RemsPharm, LLC
2. Successfully complete the Knowledge Assessment for Pharmacists
3. Complete and submit this Pharmacy Enrollment along with the completed Knowledge Assessment for Pharmacists
4. Implement the necessary staff training in a process to comply with the REMS requirements

Pharmacy Information

Organizational NPI Number

[ ] Use organizational NPI to populate form [ ] Organizational NPI Number

[ ] Office Address [ ] Mailing Address

Pharmacy Name

DEA Number

Address Line 1

Address Line 2

City State Zip Code

Number Daytime Extension Fax

The name, location, and phone number of your pharmacy will be publicly available on Clozapine REMS. If you do not want your information available, please call the Clozapine REMS Contact Center at 855-658-REMS.

A list of pharmacies located in the Clozapine REMS is available at:
- Specialty Pharmacy
- Retail Pharmacy

Authorized Responsible Information

First Name

Last Name

Credentials

[ ] DEA [ ] PharmD [ ] BCPS [ ] Other

Position or Title

Extension Fax Email

Preferred Method of Contact

[ ] Fax [ ] Text [ ] Call

Pharmacy Responsible Person—Representative Responsibilities

Pharmacy Type: (Pharmacists or Pharmacy Type. Pharmacies have different REMS requirements.)

[ ] Network Pharmacist [ ] Satellite Pharmacist

As the Authorized Representative, I must:
- Review Clozapine and the Role of Neutropenia: A Guide for Pharmacists
- Successfully complete the Knowledge Assessment for Pharmacists and submit in the Clozapine REMS
- Establish processes and procedures to verify an available, not ANC below the acceptable range for patients enrolled but not authorized to receive
- Verify all relevant staff involved in dispensing clozapine are aware of the requirements of the Clozapine REMS using the Clozapine REMS and the Role of Neutropenia, A Guide for Pharmacists

Before dispensing, all pharmacy staff must:
- Verify the patient is on clozapine and authorized to receive
- Verify the patient is on clozapine and not known to have developed clozapine
- Verify the patient is on clozapine and the box is not ANC below the acceptable range for patients enrolled but not authorized to receive
- Verify that all relevant staff involved in dispensing clozapine are aware of the requirements of the Clozapine REMS

All pharmacy staff must:
- Notify the patient or caregiver, as well as clozapine user to certified pharmacies
- Notify the patient or caregiver, as well as clozapine user to certified pharmacies
- Notify the patient or caregiver, as well as clozapine user to certified pharmacies

To establish a certification, any Authorized Representative must:
- Complete the Clozapine REMS by reviewing Clozapine and the Role of Neutropenia: A Guide for Pharmacists, successfully completing the Knowledge Assessment for Pharmacists, and the Clozapine Pharmacy Knowledge form and submit both to the Clozapine REMS.

Sign and Return

I authorize the above signatures to be the legally binding equivalent of my handwritten signatures.
Knowledge Assessment for Pharmacists

This document provides knowledge in the area of pharmacology and is intended to be used as a tool for self-assessment. It comprises a series of statements, each followed by a question mark. The correct answer to each statement is provided at the end of the document. The statements and questions are designed to test the reader's understanding of key concepts in pharmacology.

1. Which of the following is not a characteristic of a drug? (V)
   a. Allosteric interaction with receptors
   b. Autoinhibition of endogenous hormones
   c. Antagonistic effect on neurotransmitters
   d. Activating the immune system

2. Which of the following statements about the effects of drugs is true? (V)
   a. Drugs can cause harm to the body
   b. Drugs can improve health outcomes
   c. Drugs can cause addiction
   d. All of the above

3. Which of the following is not a role of pharmacists? (V)
   a. Prescribing medications
   b. Providing patient education
   c. Monitoring patient outcomes
   d. Conducting clinical trials

4. Which of the following is not a type of medication? (V)
   a. Antibiotics
   b. Antidepressants
   c. Antihistamines
   d. Antacids

5. Which of the following statements about drug interactions is true? (V)
   a. Drug interactions are always predictable
   b. Drug interactions can be minimized by using alternative medications
   c. Drug interactions are not significant in clinical practice
   d. All of the above

6. Which of the following statements about the pharmacokinetics of drugs is true? (V)
   a. Drugs are absorbed in the small intestine
   b. Drugs are eliminated by the liver
   c. Drugs are stored in body fat
   d. All of the above

7. Which of the following statements is not true about drug metabolism? (V)
   a. Drugs are metabolized in the liver
   b. Drugs are metabolized in the kidneys
   c. Drugs are metabolized in the stomach
   d. All of the above

8. Which of the following statements about drug disposition is true? (V)
   a. Drugs are disposed of by excretion
   b. Drugs are disposed of by distribution
   c. Drugs are disposed of by metabolism
   d. All of the above

9. Which of the following statements about drug elimination is true? (V)
   a. Drugs are eliminated by excretion
   b. Drugs are eliminated by distribution
   c. Drugs are eliminated by metabolism
   d. All of the above

10. Which of the following statements about drug toxicity is true? (V)
    a. Drug toxicity is determined by the dose
    b. Drug toxicity is determined by the duration of exposure
    c. Drug toxicity is determined by the route of administration
    d. All of the above

11. Which of the following statements about drug safety is true? (V)
    a. Drug safety is determined by the drug's efficacy
    b. Drug safety is determined by the drug's side effects
    c. Drug safety is determined by the drug's interactions
    d. All of the above

12. Which of the following statements about drug regulations is true? (V)
    a. Drug regulations are developed by the Food and Drug Administration (FDA)
    b. Drug regulations are developed by the Centers for Medicare and Medicaid Services (CMS)
    c. Drug regulations are developed by the Department of Health and Human Services (HHS)
    d. All of the above

13. Which of the following statements about drug development is true? (V)
    a. Drug development is a process that involves identifying a drug's potential for treatment
    b. Drug development is a process that involves testing a drug's safety and efficacy
    c. Drug development is a process that involves gaining FDA approval
    d. All of the above

14. Which of the following statements about drug marketing is true? (V)
    a. Drug marketing is the process of promoting a drug's uses and benefits
    b. Drug marketing is the process of acquiring a drug's patent
    c. Drug marketing is the process of creating a drug's brand identity
    d. All of the above

15. Which of the following statements about drug reimbursement is true? (V)
    a. Drug reimbursement is determined by the patient's insurance
    b. Drug reimbursement is determined by the drug's cost
    c. Drug reimbursement is determined by the drug's effectiveness
    d. All of the above

16. Which of the following statements about drug utilization is true? (V)
    a. Drug utilization is the process of measuring a drug's sales
    b. Drug utilization is the process of measuring a drug's distribution
    c. Drug utilization is the process of measuring a drug's prescription
    d. All of the above

17. Which of the following statements about drug resistance is true? (V)
    a. Drug resistance is the result of genetic mutations
    b. Drug resistance is the result of environmental factors
    c. Drug resistance is the result of patient compliance
    d. All of the above

18. Which of the following statements about drug development is true? (V)
    a. Drug development is a process that involves identifying a drug's potential for treatment
    b. Drug development is a process that involves testing a drug's safety and efficacy
    c. Drug development is a process that involves gaining FDA approval
    d. All of the above

19. Which of the following statements about drug marketing is true? (V)
    a. Drug marketing is the process of promoting a drug's uses and benefits
    b. Drug marketing is the process of acquiring a drug's patent
    c. Drug marketing is the process of creating a drug's brand identity
    d. All of the above

20. Which of the following statements about drug reimbursement is true? (V)
    a. Drug reimbursement is determined by the patient's insurance
    b. Drug reimbursement is determined by the drug's cost
    c. Drug reimbursement is determined by the drug's effectiveness
    d. All of the above

21. Which of the following statements about drug utilization is true? (V)
    a. Drug utilization is the process of measuring a drug's sales
    b. Drug utilization is the process of measuring a drug's distribution
    c. Drug utilization is the process of measuring a drug's prescription
    d. All of the above

22. Which of the following statements about drug resistance is true? (V)
    a. Drug resistance is the result of genetic mutations
    b. Drug resistance is the result of environmental factors
    c. Drug resistance is the result of patient compliance
    d. All of the above
### Pharmacy Personnel

A pharmacy can have multiple personnel with online accounts. You may invite personnel or remove them. You may add an authorized representative or staff to your pharmacy.

Large chain pharmacies may call the Clozapine REMS Contact Center at 1-888-558-0756 to arrange for a bulk upload of staff.

**Add Authorized Representative or Staff**

<table>
<thead>
<tr>
<th>Action</th>
<th>Role</th>
<th>Name</th>
<th>Email Address</th>
<th>Status</th>
<th>Added</th>
<th>Days Inactive</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>RxInPatJane AuthRepDoe</td>
<td><a href="mailto:RxAuthRepInPatJane@examotone.net">RxAuthRepInPatJane@examotone.net</a></td>
<td>Certified as of 6/23/2021</td>
<td>6/23/2021</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>RxInPatSally Stafflone</td>
<td><a href="mailto:RxStaffInPatSally1@examotone.net">RxStaffInPatSally1@examotone.net</a></td>
<td>Authorized</td>
<td>6/23/2021</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>RxInPatJohn StaffSmith</td>
<td><a href="mailto:RxStaffInPatJohn@examotone.net">RxStaffInPatJohn@examotone.net</a></td>
<td>Authorized</td>
<td>6/23/2021</td>
<td>1</td>
</tr>
</tbody>
</table>

Showing 1 to 3 of 3 entries

[Previous] [1] [Next]
Additional Staff

Personnel Type:
- [ ] Authorized Representative
- [x] Pharmacy Staff

Pharmacy Staff Information

Email
Email

First Name
Last Name
Title

Phone
Ext.
Fax

Cancel
Send Invite

To report any SUSPECTED ADVERSE REACTIONS, contact the Clozapine REMS Contact Center at 1-888-586-0758 or FDA at 1-800-FDA-1088 or http://www.fda.gov/medwatch
Pharmacies

A pharmacy can have multiple pharmacies grouped together under the responsibility of a Pharmacy Authorized Representative. You may add, remove, or edit the pharmacies in this pharmacy group.

Large chain pharmacies may call the Clozapine REMS Contact Center at 1-888-586-0758 to arrange for a bulk upload of stores.

<table>
<thead>
<tr>
<th>Action</th>
<th>NPI</th>
<th>Name</th>
<th>Pharmacy Type</th>
<th>Consumer Type</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>✗</td>
<td>2120000003</td>
<td>Pharmacy Calkins-Torphy</td>
<td>Inpatient Pharmacy</td>
<td>Inpatient</td>
<td>Certified as of 6/23/2021</td>
</tr>
<tr>
<td>✗</td>
<td>2120000001</td>
<td>Pharmacy D'Amore, Henmiann and Dach</td>
<td>Inpatient Pharmacy</td>
<td>Inpatient</td>
<td>Certified as of 6/23/2021</td>
</tr>
<tr>
<td>✗</td>
<td>2120000000</td>
<td>Pharmacy Herriman-Treutel</td>
<td>Inpatient Pharmacy</td>
<td>Inpatient</td>
<td>Certified as of 6/23/2021</td>
</tr>
<tr>
<td>✗</td>
<td>2120000002</td>
<td>Pharmacy Bogish Group</td>
<td>Inpatient Pharmacy</td>
<td>Inpatient</td>
<td>Certified as of 6/23/2021</td>
</tr>
</tbody>
</table>

Showing 1 to 4 of 4 entries

[Prev] 1 [Next]
Submit a Patient's ANC Lab Value

Pharmacists in possession of a patient's ANC lab value are encouraged to enter it into the Clozapine REMS. A submitted ANC lab will be visible to the patient's prescriber and pharmacy personnel attempting to obtain an RDA.

Find an enrolled patient:

Find a patient by entering the patient's information below:

<table>
<thead>
<tr>
<th>First Name</th>
<th>Last Name</th>
<th>Date of Birth</th>
</tr>
</thead>
<tbody>
<tr>
<td>REMS Patient ID</td>
<td>Phone Or Email</td>
<td></td>
</tr>
<tr>
<td>REMS Patient ID</td>
<td>Phone Or Email</td>
<td></td>
</tr>
</tbody>
</table>

Clear  Find  Cancel  Continue
Submit a Patient's ANC Lab Value
Pharmacists in possession of a patient's ANC lab value are encouraged to enter it into the Clozapine REMS. A submitted ANC lab will be visible to the patient's prescriber and pharmacy personnel attempting to obtain an RDA.

<table>
<thead>
<tr>
<th>Patient (Population: General)</th>
<th>Enrolled as of 4/17/2020</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name: Patient Hosp Pat Smith</td>
<td>Zip Code: 52722</td>
</tr>
<tr>
<td>Date of Birth: 6/27/1954</td>
<td>Phone: 920-723-6334</td>
</tr>
<tr>
<td>REMS Patient ID: CPPatEg30Cg180</td>
<td>Email: <a href="mailto:CPHspPatEg30Cg180@examoto.net">CPHspPatEg30Cg180@examoto.net</a></td>
</tr>
</tbody>
</table>

### Monitoring History

<table>
<thead>
<tr>
<th>Date</th>
<th>Monitoring Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>03/28/2021</td>
<td>Monitoring Frequency - Monthly</td>
</tr>
<tr>
<td>09/04/2020</td>
<td>ANC Lab Value - Mild Neutropenia (1000 to 1499/µL)</td>
</tr>
</tbody>
</table>

### ANC Entry

Current Patient Monitoring Frequency: Monthly

<table>
<thead>
<tr>
<th>Blood Draw Date</th>
<th>General Patient Population</th>
<th>ANC (per µL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MM/DD/YYYY</td>
<td>Normal Range (≥ 1500/µL)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mild Neutropenia (1000 to 1499/µL)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Moderate Neutropenia (500 to 999/µL)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Severe Neutropenia (&lt; 500/µL)</td>
<td></td>
</tr>
</tbody>
</table>

[Cancel] [Save]
Obtain a Patient’s REMS Dispense Authorization (RDA)
An RDA is a receipt from the Clozapine REMS signifying that the REMS requirements to dispense for this patient are currently met. Find an enrolled patient:

Find a patient by entering the patient’s information below:

<table>
<thead>
<tr>
<th>First Name</th>
<th>Last Name</th>
<th>Date of Birth</th>
</tr>
</thead>
<tbody>
<tr>
<td>REMS Patient ID</td>
<td>Phone Or Email</td>
<td></td>
</tr>
<tr>
<td>REMS Patient ID</td>
<td>Phone Or Email</td>
<td></td>
</tr>
</tbody>
</table>

Clear  Find  Cancel  Continue
Obtain a Patient's REMS Dispense Authorization (RDA)

An RDA is a receipt from the Clozapine REMS signifying that the REMS requirements to dispense for this patient are currently met.

Find an enrolled patient:

1. Find a patient by entering the patient's information below:

   **First Name**
   
   **Last Name**
   
   **Date of Birth**

   **REMS Patient ID**
   
   **Phone Or Email**

   **First Name**
   
   **REMS Patient ID**
   
   **Telephone**

   * There are errors, please correct the items below:

   - The patient cannot be found with the data entered. Enter additional data or contact the Clozapine REMS Contact Center at 1-844-267-8678

   [Clear] [Find] [Cancel] [Continue]
Obtain a Patient's REMS Dispense Authorization (RDA)
An RDA is a receipt from the Clozapine REMS signifying that the REMS requirements to dispense for this patient are currently met.
Find an enrolled patient:

1. Find a patient by entering the patient's information below:

   - **First Name**
   - **Last Name**
   - **Date of Birth**

   - **First Name**
   - **Smith**
   - **mm/dd/yyyy**

   - **REMS Patient ID**
   - **Phone Or Email**

   - **REMS Patient ID**
   - **Phone Or Email**

   - **There are errors, please correct the items below:**

     - The search result returned too many rows. Please enter additional data to narrow the search.

   - **Clear**
   - **Find**

   - **Cancel**
   - **Continue**
Obtain a Patient’s REMS Dispense Authorization (RDA)

An RDA is a receipt from the Clozapine REMS signifying that the REMS requirements to dispense for this patient are currently met.
Find an enrolled patient:

1. Find a patient by entering the patient’s information below:

<table>
<thead>
<tr>
<th>First Name</th>
<th>Last Name</th>
<th>Date of Birth</th>
</tr>
</thead>
<tbody>
<tr>
<td>First Name</td>
<td>Smitt</td>
<td>mm/dd/yyyy</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>REMS Patient ID</th>
<th>Phone Or Email</th>
</tr>
</thead>
<tbody>
<tr>
<td>REMS Patient ID</td>
<td>Phone Or Email</td>
</tr>
</tbody>
</table>

2 results found
- Patient Terri Smitt (DOB: 2/19/1970)
- Patient Terry Smitt (DOB: 9/22/1989)
Obtain a Patient's REMS Dispense Authorization (RDA)
An RDA is a receipt from the Clozapine REMS signifying that the REMS requirements to dispense for this patient are currently met.

Find an enrolled patient:

<table>
<thead>
<tr>
<th>First Name</th>
<th>Last Name</th>
<th>Date of Birth</th>
</tr>
</thead>
<tbody>
<tr>
<td>First Name</td>
<td>Smitt</td>
<td>mm/dd/yyyy</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>REMS Patient ID</th>
<th>Phone Or Email</th>
</tr>
</thead>
<tbody>
<tr>
<td>REMS Patient ID</td>
<td>Phone Or Email</td>
</tr>
</tbody>
</table>

2 results found
- Patient Terri Smitt (DOB: 2/19/1970)
- Patient Terry Smitt (DOB: 9/22/1989)
Obtain a Patient's REMS Dispense Authorization (RDA)

An RDA is a receipt from the Clozapine REMS signifying that the REMS requirements to dispense for this patient are currently met.

**Patient**

- **Name:** Patient Terry Smitt
- **Date of Birth:** 9/22/1989
- **REMS Patient ID:** CP1378924

**Enrolled as of 11/23/2020**

- **Zip Code:** 28601
- **Phone:** 920-723-6334
- **Email:** CPPatientGE01@examoto.net

**REMS Dispense Authorization (RDA)**

A REMS Dispense Authorization is a receipt from the Clozapine REMS indicating that the safe use conditions managed by the REMS are currently in place. After obtaining an RDA, retain it as your receipt.

**Obtain RDA**

**Cancel**
Obtain a Patient's REMS Dispense Authorization (RDA)

An RDA is a receipt from the Clozapine REMS signifying that the REMS requirements to dispense for this patient are currently met.

Patient (Population: General)

Name: Patient Terry Smith
Date of Birth: 9/22/1989
REMS Patient ID: CPPatE130NoC

Zip Code: 28601
Phone: 920-723-6334
Email: CPPatE130NoC@examoto.net

Enrolled as of 3/23/2021

REMS Dispense Authorization (RDA)

A REMS Dispense Authorization is a receipt from the Clozapine REMS indicating that the safe use conditions managed by the REMS are currently in place. After obtaining an RDA, retain it as your receipt.

RDA: a620091f

Obtained by RxOutPatJane AuthRep Doe on 04/13/2021 at 11:57 AM Coordinated Universal Time

Dispensing Information

Outpatients should be dispensed a days' supply in accordance with their monitoring frequency.

Date: mm/dd/yyyy
Manufacturer:
NDC Code:
Days' Supply:
Quantity:

Save
Obtain a Patient's REMS Dispense Authorization (RDA)

An RDA is a receipt from the Clozapine REMS signifying that the REMS requirements to dispense for this patient are currently met.

**Patient** (Population: General)  
Enrolled as of 3/22/2021

<table>
<thead>
<tr>
<th>Name:</th>
<th>Patient Terry Smitt</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of Birth:</td>
<td>9/22/1969</td>
</tr>
<tr>
<td>REMS Patient ID:</td>
<td>CPhEti3NoC</td>
</tr>
</tbody>
</table>

**Rems Dispense Authorization (RDA)**

A REMS Dispense Authorization is a receipt from the Clozapine REMS indicating that the safe use conditions managed by the REMS are currently in place. After obtaining an RDA, retain it as your receipt.

RDA: a620091f

Obtained by RxOutPatJane.AuthRepDoe on 04/13/2021 at 11:57 AM Coordinated Universal Time

**Safe Use Conditions:**
- Patient is Enrolled: Patient Terry Smitt
- Pharmacy is Certified

**Dispensing Information**

Outpatients should be dispensed a days' supply in accordance with their monitoring frequency.

<table>
<thead>
<tr>
<th>Date</th>
<th>Manufacturer</th>
<th>NDC Code</th>
<th>Days' Supply</th>
<th>Quantity</th>
</tr>
</thead>
<tbody>
<tr>
<td>mm/dd/yyyy</td>
<td>Manufacturers</td>
<td>NDC Codes</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Obtain a Patient’s REMS Dispense Authorization (RDA)

An RDA is a receipt from the Clozapine REMS signifying that the REMS requirements to dispense for this patient are currently met.

**Patient (Population: General)**

<table>
<thead>
<tr>
<th>Name:</th>
<th>Patient Pat Smith</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of Birth:</td>
<td>7/15/1965</td>
</tr>
<tr>
<td>REMS Patient ID:</td>
<td>C9PatEg30C137</td>
</tr>
</tbody>
</table>

**Enrolled as of 2/11/2021**

**REMS Dispense Authorization (RDA)**

A REMS Dispense Authorization is a receipt from the Clozapine REMS indicating that the safe use conditions managed by the REMS are currently in place. After obtaining an RDA, retain it as your receipt.

RDA: c64d99ef

Obtained by RxOutPatJane AuthRepDoe on 04/13/2021 at 12:30 PM Coordinated Universal Time

**Safe Use Conditions:**
- Patient is Enrolled: Patient Pat Smith
- Patient, Patient Pat Smith, has a current Patient Status Form (PSF) on file indicating the patient is continuing treatment.
- Pharmacy is Certified

**Dispensing Information**

Outpatients should be dispensed a days’ supply in accordance with their monitoring frequency.

<table>
<thead>
<tr>
<th>Date</th>
<th>Manufacturer</th>
<th>NDC Code</th>
<th>Days’ Supply</th>
<th>Quantity</th>
</tr>
</thead>
<tbody>
<tr>
<td>mm/dd/yyyy</td>
<td>Manufacturers</td>
<td>NDC Codes</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Save
Obtain a Patient’s REMS Dispense Authorization (RDA)

An RDA is a receipt from the Clozapine REMS signifying that the REMS requirements to dispense for this patient are currently met.

**Patient (Population: General)**

Name: PatientPat Smithe  
Date of Birth: 6/27/1954  
REMS Patient ID: CPDemoPatDiscont  
Zip Code: 44145  
Phone: 204-896-7543  
Email: CPPatDiscont@examot.net  
Enrolled as of 2/11/2021

**REMS Dispense Authorization (RDA)**

A REMS Dispense Authorization is a receipt from the Clozapine REMS indicating that the safe use conditions managed by the REMS are currently in place. After obtaining an RDA, retain it as your receipt.

⚠️ **DO NOT DISPENSE**

**Safe Use Conditions:**

- Patient is Enrolled: PatientPat Smithe
- Patient, PatientPat Smithe, most recent Patient Status Form (PSF) on file indicates the patient has discontinued treatment. Let the patient know that their prescriber has not authorized a refill and to contact their prescriber if necessary.
- Pharmacy is Certified

Cancel
**Obtain a Patient's REMS Dispense Authorization (RDA)**

An RDA is a receipt from the Clozapine REMS signifying that the REMS requirements to dispense for this patient are currently met.

<table>
<thead>
<tr>
<th>Patient (Population: General)</th>
<th>Enrolled as of 2/11/2021</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name: PatientAli Smithson</td>
<td>Zip Code: 35405</td>
</tr>
<tr>
<td>Date of Birth: 4/4/1962</td>
<td>Phone: 920-727-6902</td>
</tr>
<tr>
<td>REMS Patient ID: CPPatInterrupt</td>
<td>Email: <a href="mailto:CPPatInterrupt@examoto.net">CPPatInterrupt@examoto.net</a></td>
</tr>
</tbody>
</table>

**REMS Dispense Authorization (RDA)**

A REMS Dispense Authorization is a receipt from the Clozapine REMS indicating that the safe use conditions managed by the REMS are currently in place. After obtaining an RDA, retain it as your receipt.

**DO NOT DISPENSE**

**Detail**

**Safe Use Conditions:**

- ✔ Patient is Enrolled: PatientAli Smithson
- ❌ Patient, PatientAli Smithson, most recent Patient Status Form (PSF) on file indicates the patient has interrupted treatment. Let the patient know that their prescriber has not authorized a refill and to contact their prescriber if necessary.
- ✔ Pharmacy is Certified

**To report any SUSPECTED ADVERSE REACTIONS, contact the Clozapine REMS Contact Center at 1-888-566-0758 or FDA at 1-800-FDA-1088 or http://www.fda.gov/medwatch.**
Obtain a Patient’s REMS Dispense Authorization (RDA)

An RDA is a receipt from the Clozapine REMS indicating that the REMS requirements to dispense for this patient are currently met.

**Patient (Population: General)***

<table>
<thead>
<tr>
<th>Name</th>
<th>Patient Pat Smith</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of Birth</td>
<td>6/27/1954</td>
</tr>
<tr>
<td>REMS Patient ID</td>
<td>CPPatEg930Cg37</td>
</tr>
</tbody>
</table>

**Zip Code:** 52722  
**Phone:** 920-723-6334  
**Email:** CPPatEg930Cg37@exam.com

**REMS Dispense Authorization (RDA)**

A REMS Dispense Authorization is a receipt from the Clozapine REMS indicating that the safe use conditions managed by the REMS are currently in place. After obtaining an RDA, retain it as your receipt.

**DO NOT DISPENSE**

**Detail**

- **Safe Use Conditions:**
  - Patient is Enrolled: Patient Pat Smith
  - Patient, Patient Pat Smith, does NOT have a current Patient Status Form (PSF) on file. If you have a current ANC Lab value, you may request a Pharmacy Dispense Rationale for this patient below.
  - Pharmacy is Certified

**Recent Monitoring History**

<table>
<thead>
<tr>
<th>Date</th>
<th>Monitoring Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>03/28/2021</td>
<td>Monitoring Frequency - Monthly</td>
</tr>
<tr>
<td>03/25/2021</td>
<td>ANC Lab Value - Mild Neutropenia (1000 to 1499/µL)</td>
</tr>
<tr>
<td>03/10/2021</td>
<td>ANC Lab Value - Not Reported (Clinician Discretion)</td>
</tr>
<tr>
<td>02/24/2021</td>
<td>ANC Lab Value - Normal Range (≤ 1500/µL)</td>
</tr>
<tr>
<td>02/17/2021</td>
<td>ANC Lab Value - Not Reported (Clinician Discretion)</td>
</tr>
</tbody>
</table>

Showing 1 to 5 of 7 entries

**Pharmacy Dispense Rationale Information**

- **Prescriber NPI on patient’s script:**
- **Blood Draw Date:** MM/DD/YYYY
- **ANC (per µL):** 0

**Request Dispense Rationale**
**Obtain a Patient’s REMS Dispense Authorization (RDA)**

An RDA is a receipt from the Clozapine REMS signifying that the REMS requirements to dispense for this patient are currently met.

<table>
<thead>
<tr>
<th><strong>Patient (Population: General)</strong></th>
<th><strong>Enrolled as of 4/17/2020</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Name: PatientHospPat Smith</td>
<td></td>
</tr>
<tr>
<td>Date of Birth: 6/27/1954</td>
<td></td>
</tr>
<tr>
<td>REMS Patient ID: CPPatEg30Cg180</td>
<td></td>
</tr>
<tr>
<td>Zip Code: 52722</td>
<td></td>
</tr>
<tr>
<td>Phone: 920-723-6334</td>
<td></td>
</tr>
<tr>
<td>Email: <a href="mailto:CPHspPatEg30Cg180@examoto.net">CPHspPatEg30Cg180@examoto.net</a></td>
<td></td>
</tr>
</tbody>
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**REMS Dispense Authorization (RDA)**

A REMS Dispense Authorization is a receipt from the Clozapine REMS indicating that the safe use conditions managed by the REMS are currently in place. After obtaining an RDA, retain it as your receipt.

**⚠️ DO NOT DISPENSE**

**Detail**

1. **Safe Use Conditions:**
   - Patient is Enrolled: PatientHospPat Smith
   - General population Patient, PatientHospPat Smith, has a Dispense Rationale with an ANC greater than 999 per μL
   - Pharmacy is Certified
   - Patient, PatientHospPat Smith, has reached the Dispense Rationale limit. Please contact the patient’s prescriber, the prescriber is required to submit a Patient Status Form (PSF) for this patient to receive drug.
   - Prescriber is Certified: PRJane PRDoe

**Cancel**
Obtain a Patient's REMS Dispense Authorization (RDA)

An RDA is a receipt from the Clozapine REMS signifying that the REMS requirements to dispense for this patient are currently met.

**Patient (Population: General)**

<table>
<thead>
<tr>
<th>Name</th>
<th>Terry Smith</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of Birth</td>
<td>9/22/1989</td>
</tr>
<tr>
<td>REMS Patient ID</td>
<td>CPPatEi30NoC</td>
</tr>
<tr>
<td>Zip Code</td>
<td>28601</td>
</tr>
<tr>
<td>Phone</td>
<td>920-723-6334</td>
</tr>
<tr>
<td>Email</td>
<td><a href="mailto:CPPatEi30NoC@examoto.net">CPPatEi30NoC@examoto.net</a></td>
</tr>
</tbody>
</table>

**REMS Dispense Authorization (RDA)**

A REMS Dispense Authorization is a receipt from the Clozapine REMS indicating that the safe use conditions managed by the REMS are currently in place. After obtaining an RDA, retain it as your receipt.

- **RDA:** ee9ad14d
- **Copy**
- **Print**

Obtained by RxOutPatJane AuthRepDoe on 04/13/2021 at 12:25 PM Coordinated Universal Time.

**Detail**

- Prescription dispense recorded for this RDA.
Obtain a Patient's REMS Dispense Authorization (RDA)

An RDA is a receipt from the Clozapine REMS signifying that the REMS requirements to dispense for this patient are currently met.

**Patient (Population: General)**

<table>
<thead>
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<th>Patient Terry Smith</th>
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<tr>
<td>REMS Patient ID:</td>
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</tr>
<tr>
<td>Zip Code:</td>
<td>28601</td>
</tr>
<tr>
<td>Phone:</td>
<td>920-223-6334</td>
</tr>
<tr>
<td>Email:</td>
<td><a href="mailto:CPPatEl30NoC@examoto.net">CPPatEl30NoC@examoto.net</a></td>
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**REMS Dispense Authorization (RDA)**

A REMS Dispense Authorization is a receipt from the Clozapine REMS indicating that the safe use conditions managed by the REMS are currently in place. After obtaining an RDA, retain it as your receipt.

- RDA Reversed.