FDA is temporarily exercising enforcement discretion with respect to certain Clozapine REMS program requirements to ensure continuity of care for patients taking clozapine

[Updated 11/02/2022] FDA is temporarily exercising additional enforcement discretion with respect to certain Clozapine REMS program requirements to ensure continuity of care for patients taking clozapine. FDA is aware health care professionals and patients continue to experience ongoing difficulties with the Clozapine REMS program, including issues with patient access to clozapine for patients recently discharged from an inpatient setting. To address the concern that inpatient pharmacies are only allowed to dispense a 7-days' supply of clozapine to the patient upon discharge, FDA does not intend to object if:

- Inpatient pharmacies dispense a days' supply of clozapine that aligns with the patient's monitoring frequency (e.g., weekly monitoring = 7 days' supply, twice monthly monitoring = 14 days' supply, monthly monitoring = 30 days' supply) upon discharge from an inpatient facility.

FDA continues to exercise the enforcement discretion announced in November 2021, including FDA does not intend to object if:

- Pharmacists dispense clozapine without a REMS dispense authorization (RDA).
- Wholesalers ship clozapine to pharmacies and health care settings without confirming enrollment in the REMS.

Abrupt discontinuation of clozapine can result in significant complications for patient treatment. Health care professionals should use their clinical judgment with regard to prescribing and dispensing clozapine to patients with an absolute neutrophil count (ANC) within the acceptable range.

We understand that difficulties with the Clozapine REMS program have caused frustration and have led to problems with patient access to clozapine. FDA takes these concerns seriously. Continuity of care, patient access to clozapine, and patient safety are our highest priorities. We are working closely with the Clozapine REMS program administrators to address these challenges and to avoid interruptions in patient care.

We encourage pharmacists and prescribers to continue working with the Clozapine REMS to complete certification and prescribers should continue to enroll patients and submit the Patient Status Form.

If you have questions or concerns about the Clozapine REMS Program or its website, please contact FDA at druginfo@fda.hhs.gov (mailto:druginfo@fda.hhs.gov), 1-855-543-3784 or 301-796-3400.

[Updated 12/2/2021] Health care professionals continue to alert FDA about ongoing difficulties with the Clozapine REMS program (http://www.clozapinerems.com/) (http://www.fda.gov/about-fda/website-policies/website-disclaimer), including a high call volume and long call wait times for stakeholders since launch of the program on November 15, 2021. We understand that this has caused frustration and has led to patient access issues for clozapine. FDA takes these concerns seriously. Continuity

of care, patient access to clozapine, and patient safety are our highest priorities. We are working closely with the Clozapine REMS program administrators to address these challenges and avoid interruptions in patient care.

Due to problems with implementation of the Clozapine REMS program and the potential impact to patient care, FDA does not intend to object if:

- **Pharmacists** dispense clozapine without a REMS dispense authorization (RDA).
- **Wholesalers** ship clozapine to pharmacies and health care settings without confirming enrollment in the REMS

Abrupt discontinuation of clozapine can result in significant complications for patient treatment. Health care professionals should use their clinical judgment with regard to prescribing and dispensing clozapine to patients with an absolute neutrophil count (ANC) within the acceptable range.

We encourage pharmacists and prescribers to continue working with the Clozapine REMS to complete certification and patient enrollment.

If you have questions or concerns about the Clozapine REMS Program or its website, please contact FDA at druginfo@fda.hhs.gov (mailto:druginfo@fda.hhs.gov), 1-855-543-3784 or 301-796-3400.

[Updated 7/29/21] CPMG and FDA continue to work to ensure that patients relying on clozapine have continued access to this medication and appropriate management of associated risks.

On July 29, 2021, FDA approved a modification to the Clozapine REMS. The modification to Clozapine REMS will go into effect on November 15, 2021. Important changes include:

- **All prescribers and pharmacies must be re-certified** by November 15, 2021, or they will no longer be able to prescribe/dispense clozapine.
- **Prescribers must re-enroll their patients** who will continue clozapine by November 15, 2021. Patients who are not re-enrolled by that day will no longer be able to receive clozapine.
- Re-certification and re-enrollment can begin on August 16, 2021.
- Pharmacies will no longer be able to use the telecommunication verification (also known as the switch system) to verify safe use conditions. The authorization to dispense will be obtained either through the contact center or online via the REMS website.
- A new **Patient Status Form** will document absolute neutrophil count (ANC) monitoring for all outpatients. This form must be submitted monthly. Patient monitoring must continue per the Prescribing Information.

To re-certify and re-enroll in the Clozapine REMS please see the Important Program Update (https://www.clozapinerems.com/CpmgClozapineUI/home.u) (http://www.fda.gov/about-fda/website-policies/website-disclaimer) at www.clozapinerems.com (http://www.clozapinerems.com)

(http://www.fda.gov/about-fda/website-policies/website-disclaimer) More information on these changes and other Clozapine REMS requirements are included below.

Effective November 15, 2021, the Clozapine REMS requires:

For prescribers who prescribe for outpatient use or prescribers who are initiating treatment inpatient:

- Certify in the Clozapine REMS program
- Counsel the patient on the risk of severe neutropenia and enroll patients in the Clozapine REMS program
- Obtain and assess the patient's ANC in accordance to the patient's monitoring frequency in the clozapine Prescribing Information
- Document the ANC on the Patient Status Form and submit this form monthly.
    - Patient monitoring must still continue per the Prescribing Information.
    - If an ANC is missing, the prescriber is required to provide authorization to continue therapy.
    - A Patient Status Form must be received within 37 calendar days after the date of the first dispensing or the last Patient Status Form.
    - A Patient Status Form will 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

For pharmacies that dispense clozapine for outpatient use:

- Certify in the Clozapine REMS
- Obtain a REMS Dispense Authorization (RDA) prior to each dispense utilizing either the REMS website or calling the REMS Contact Center.
    - For the first dispensing, the RDA will verify that the pharmacy is certified, patient is enrolled, and patient's treatment is not interrupted or discontinued
    - For subsequent dispensing, the RDA will verify that the pharmacy is certified, patient is enrolled, a Patient Status Form has been completed in the last 37 days, and patient's treatment is not interrupted or discontinued

For pharmacies that dispense clozapine for inpatient use:

- Certify in the Clozapine REMS
- Obtain a REMS Dispense Authorization (RDA) prior to the initial dispense utilizing either the REMS website or calling the REMS Contact Center. The RDA will verify that the pharmacy is certified, patient is enrolled, and patient's treatment is not interrupted or discontinued

For additional information about the Clozapine REMS, please call the Clozapine REMS Contact Center at 844-267-8678 or visit www.clozapinerems.com (http://www.clozapinerems.com) (http://www.fda.gov/about-fda/website-policies/website-disclaimer).

Beginning August 16, 2021, a Transition Contact Center will be available to support re-certification, re-enrollment activities and to answer questions at 888-586-0758.

[Updated 1/16/19] The Clozapine Product Manufacturers' Group (CPMG) and the U.S. Food and Drug Administration (FDA) continue to work to ensure that patients relying on clozapine have continued access to this medication and appropriate management of associated risks.

As a result of this work, a modification to Clozapine REMS Program will be effective February 28, 2019. Important highlights of this modification are that:

- Prescribers and pharmacies must be certified by February 28, 2019 or they will no longer be able to prescribe/dispense clozapine,
- Inpatient prescribers are not required to be certified if they are prescribing for patients already enrolled in the program,
- If a patient's absolute neutrophil count (ANC) is not current, this will not prevent clozapine from being dispensed, and
- Pharmacies are no longer allowed to enroll patients in the Clozapine REMS Program after February 28, 2019, since the enrollment of patients must be completed by the prescriber or the prescriber designee.

More information on these and other Clozapine REMS Program requirements is included below.

For specific instructions related to the Clozapine REMS Program please see the Important Program Update (https://www.clozapinerems.com/CpmgClozapineUI/home.u) (http://www.fda.gov/about-fda/website-policies/website-disclaimer) issued by CPMG.

Effective February 28, 2019, the Clozapine REMS Program requirements are:

- Prescribers who prescribe clozapine for **outpatient** use must:
    - Certify in the Clozapine REMS Program
        - If you need to prescribe clozapine but are ***not yet*** certified in the Clozapine REMS Program, go immediately to www.clozapinerems.com. Once a prescriber is certified, his/her prescriber designees must also enroll online at www.clozapinerems.com (http://www.clozapinerems.com) (http://www.fda.gov/about-fda/website-policies/website-disclaimer).
    - Enroll patients in the Clozapine REMS Program
        - Patient enrollment in the Clozapine REMS Program (https://www.clozapinerems.com/CpmgClozapineUI/home.u)

(http://www.fda.gov/about-fda/website-policies/website-disclaimer) is confirmed prior to dispensing.

- If the patient is not enrolled in the Clozapine REMS Program, a dispense will not be authorized.

- Obtain an absolute neutrophil count (ANC) for patients in accordance with the clozapine Prescribing Information and aligned with the patient's monitoring frequency
  - Submit the ANC directly to the Clozapine REMS Program according to the patient's monitoring frequency (i.e. within 7, 15, or 31 days), so the current ANC is in the REMS Program database prior to the dispense.
  - If the last ANC on file for a patient indicates moderate or severe neutropenia, a dispense will not be authorized unless the prescriber documents that the benefits of clozapine outweigh the risks associated with neutropenia (i.e. . a "Treatment Rationale" is on file).
    - A *Treatment Rationale* can be submitted by logging into your account at www.clozapinerems.com (https://www.clozapinerems.com/CpmgClozapineUI/home.u) (http://www.fda.gov/about-fda/website-policies/website-disclaimer) or by calling the Clozapine REMS Program Contact Center at 844-267-8678.
  - If a patient does not have an ANC on file with the REMS, a dispense will not be authorized.

- Prescribers who prescribe clozapine for **inpatient** use:
  - Are not required to be certified if they are prescribing for patients already enrolled in the program.
  - Must enroll the patient in the Clozapine REMS Program prior to receiving their first dose if the patient is initiated on clozapine while in an inpatient setting.
  - Should use clinical judgement to determine whether the benefits of receiving clozapine outweigh the risks if a patient has an ANC indicating moderate or severe neutropenia in the inpatient setting.
- Pharmacies that dispense clozapine:
  - Must certify in the Clozapine REMS
    - If your pharmacy dispenses clozapine and is ***not yet*** certified in the Clozapine REMS Program, certify online at www.clozapinerems.com (http://www.clozapinerems.com) (http://www.fda.gov/about-fda/website-policies/website-disclaimer). Outpatient pharmacies must obtain a "Pre-Dispense Authorization" (PDA) prior to dispensing clozapine.
  - Are encouraged to submit ANCs to the Clozapine REMS Program when the pharmacist is made aware of a more current ANC.
  - Will no longer be allowed to enroll patients. Enrollment of patients must be completed by the prescriber or the prescriber designee.
  - Must complete an "Eligibility Check" prior to dispensing clozapine, if they are an inpatient pharmacy.

- Need to know that a PDA will not be issued, and an Eligibility Check will not be successful, if the patient is not enrolled in the Clozapine REMS Program.
- In outpatient settings, need to know that a PDA will not be issued if an ANC is not on file, or if a patient has an ANC that indicates moderate or severe neutropenia without a prescriber Treatment Rationale on file.
- Although not required, pharmacies are encouraged to contact the prescriber to acquire the most recent patient ANC information for patient safety purposes, if a current ANC is not on file. In the future, patients who do not have a current ANC on file may not be allowed to receive clozapine.

For additional information about the Clozapine REMS Program, please call the Clozapine REMS Program Contact Center at 844-267-8678 or visit www.clozapinerems.com (http://www.clozapinerems.com) (http://www.fda.gov/about-fda/website-policies/website-disclaimer).

[Updated 12/16/2016] Full launch for the Clozapine Risk Evaluation and Mitigation Strategy (REMS) program will not be implemented in 2016

Although the FDA announced in May 2016 that the full REMS program launch would occur in December 2016, recent technical and logistical challenges necessitate that we postpone the launch. The Clozapine Product Manufacturers' Group and the FDA are continuing to work to ensure that patients relying on clozapine have continued access to this medication and appropriate management of associated risks. We are planning a phased approach to implementing the Clozapine REMS Program in order to carefully balance patient access and ensuring the safe use of clozapine during the transition to a fully implemented Clozapine REMS Program.

Prescribers and pharmacies that have not certified in the Clozapine REMS Program are encouraged to use this additional time to certify in the program before the full launch, which includes a fully implemented predispense authorization (PDA) for pharmacies. In addition, prescribers should submit absolute neutrophil count (ANC) results to the Clozapine REMS Program according to the patients monitoring frequency (i.e. within 7, 15, or 31 days) to ensure the ANC is current. If prescribers and/or pharmacies are not certified in the Clozapine REMS Program and the ANC in the Clozapine REMS Program is not current after the full launch, this will impact the pharmacy's ability to dispense clozapine, negatively affecting patient care.

Updated information will be sent to prescribers and pharmacies once an implementation date has been confirmed.

During this extension, prescribers and pharmacies should continue to adhere to the current Clozapine REMS Program requirements:

1. Current prescriber requirements:

- **Enroll** patients in the Clozapine REMS Program
  - Patient enrollment in the Clozapine REMS Program is confirmed ***prior to*** dispensing clozapine
  - You can enroll patients through your account on www.clozapinerems.com (http://www.clozapinerems.com/) (http://www.fda.gov/about-fda/website-policies/website-

disclaimer) or by calling the Clozapine REMS Program Contact Center at 844-267-8678

- If the patient is not enrolled in the Clozapine REMS Program, a dispense will not be authorized

- **Obtain** an absolute neutrophil count (ANC) for patients in accordance with the clozapine Prescribing Information and aligned with the patients monitoring frequency
- **Submit the ANC** directly to the Clozapine REMS Program according to the patients monitoring frequency (i.e. within 7, 15, or 31 days) so the current ANC is in the REMS Program database **prior** to the dispense
  - ANCs should be submitted directly to the REMS Program and not to the pharmacy to ensure timely data entry into the system
    - ANCs may be submitted to the program by logging into your account on www.clozapinerems.com (http://www.clozapinerems.com/) (http://www.fda.gov/about-fda/website-policies/website-disclaimer) or by calling the Clozapine REMS Program Contact Center at 844-267-8678
    - ANCs may also be submitted using the ANC reporting form (available under the Resources tab on www.clozapinerems.com (http://www.clozapinerems.com/) (http://www.fda.gov/about-fda/website-policies/website-disclaimer)). However it will take up to 48 hours to process this form
  - If a patient does not have an ANC on file with the REMS, a dispense ***will not be authorized***
  - If the last ANC on file for a patient indicates moderate or severe neutropenia, a dispense ***will not be authorized***
  - A patient with an ANC that indicates moderate or severe neutropenia must have a Treatment Rationale on file before the dispense can be authorized
    - A Treatment Rationale can be submitted by logging into your account at www.clozapinerems.com (http://www.clozapinerems.com/) (http://www.fda.gov/about-fda/website-policies/website-disclaimer) or by calling the Clozapine REMS Program Contact Center at 844-267-8678
    - The ANC reporting form can also be used to submit a Treatment Rationale. However, it will take up to 48 hours to process this form

2. Current pharmacy requirements:

- Outpatient pharmacies must **obtain a PDA** prior to dispensing clozapine and inpatient pharmacies are required to **complete an eligibility check** prior to dispensing clozapine
  - A PDA will not be issued or the eligibility check will not be successful if the patient is not enrolled in the Clozapine REMS Program, if an ANC is not on file, or if a patient has an ANC that indicates moderate or severe neutropenia (without a prescriber Treatment Rationale)
  - Pharmacies may still enroll patients in the Clozapine REMS Program by calling the Clozapine REMS Program Contact Center at 844-267-8678

Currently, the following will not prevent a patient from receiving clozapine from the pharmacy:

- Prescribers and Pharmacies not certified
    - Because there are technical problems with the system that have not yet been resolved, we encourage adherence to the requirements though the absence of prescriber and pharmacy certification will not preclude a patient being dispensed clozapine**. In the future, patients that are not associated with a certified prescriber and pharmacy will not be allowed to receive clozapine.**
    - ANC not current (i.e. within 7, 15, or 31 days of the dispense date) based on the patient's monitoring frequency (MF)
        - Although not required, pharmacies are encouraged to contact the prescriber to acquire the most recent patient ANC information for patient safety purposes**. In the future, patients that do not have a current ANC on file may not be allowed to receive clozapine.**

For additional information about the Clozapine REMS Program, please call at the Clozapine REMS Program Contact Center at 844-267-8678.

[Updated 11/19/2015] Clozapine REMS deadlines for prescribers and pharmacies extended

Due to ongoing implementation challenges with the new Clozapine REMS Program, FDA is extending the November 23, 2015 prescriber certification deadline and the December 14, 2015 pharmacy certification deadline to help ensure that health care professionals have sufficient time to complete this process and that patient access to clozapine is maintained. We are also carefully evaluating next steps regarding the December 14, 2015 pre-dispense authorization (PDA) launch. We will communicate the revised certification deadlines and additional information about the PDA launch as soon as possible.

Healthcare providers should prioritize the medical needs of their patients and, as appropriate, continue prescribing and dispensing clozapine to patients with an absolute neutrophil count (ANC) within the acceptable ranges while the issues are being resolved by the Clozapine REMS program administrators. Prescribers and pharmacies should continue to work with the Clozapine REMS Program administrators to resolve any issues and continue their efforts to complete certification and update patient information to meet the requirements of the program.

[Updated 11/13/2015] FDA working with manufacturers to resolve challenges with the Clozapine REMS Program

Health care professionals continue to alert FDA about ongoing difficulties with the Clozapine REMS (http://www.clozapinerems.com/) (http://www.fda.gov/about-fda/website-policies/website-disclaimer) Program, including technical issues with the website, data migration problems, and long call wait times since the launch of the program on October 12, 2015. We understand this has caused frustration and take these concerns seriously. We are working closely with the Clozapine REMS program administrators to address the challenges, many of which are a result of merging data from six registries encompassing more than 50,000 prescribers, 28,000 pharmacies, and 90,000 patient records.

During this transition to the new shared Clozapine REMS program, continuity of care, patient access to clozapine, and patient safety are our highest priorities. Healthcare providers should prioritize the medical needs of their patients and, as appropriate, continue prescribing and dispensing clozapine to patients with an absolute neutrophil count (ANC) within the acceptable ranges while the issues are being resolved by the Clozapine REMS program administrators. Prescribers and pharmacies should continue to work with the Clozapine REMS Program to resolve any issues.

FDA has asked the Clozapine REMS Program administrators to continue posting updated information and to help answer frequently asked questions under the "Important Program Update" section of the Clozapine REMS Program (http://www.clozapinerems.com/) (http://www.fda.gov/about-fda/website-policies/website-disclaimer) homepage.

Prescribers and pharmacists who encounter issues with the Clozapine REMS Program should contact the Clozapine REMS Contact Center at 1-844-267-8678; Monday – Friday, 8am – 10pm EST. Because of the challenges mentioned above, the Contact Center has been extremely busy. However, the Clozapine REMS program administrators have informed FDA that wait times are improving. We encourage pharmacists and prescribers to continue their efforts to complete certification and update patient information to meet the requirements of the program.

If you have questions or concerns about the Clozapine REMS Program or its website please contact FDA at druginfo@fda.hhs.gov (mailto:druginfo@fda.hhs.gov), 1-855-543-3784 or 301-796-3400.

[10/20/2015] FDA alerts prescribers and pharmacists to continue clozapine prescribing and dispensing if they encounter online Clozapine REMS certification issues

Program launched October 12, 2015; technical issues resolved as of October 16, 2015

The FDA is aware that in recent days, technical difficulties with the new Clozapine REMS (http://www.clozapinerems.com/) (http://www.fda.gov/about-fda/website-policies/website-disclaimer) website have prevented some pharmacies and prescribers from completing their required online Clozapine REMS certification. This has resulted in patient access issues in some cases. The clozapine manufacturers, who are the REMS program administrators, have notified FDA that these technical issues have been resolved as of October 16, 2015. **If prescribers and pharmacists continue to experience any issues, they should use clinical judgment and consider the best interests of the patient. Continue prescribing and dispensing clozapine to patients with an absolute neutrophil count (ANC) within the acceptable ranges while the issues are being resolved.**

Prescribers and authorized representatives for pharmacies who encountered certification difficulties should resume the online certification process. Pharmacists at chain pharmacies will be receiving additional communication from their authorized representative.

Prescribers or pharmacists who continue to encounter technical issues with the Clozapine REMS Program should contact the Clozapine REMS Contact Center at 1-844-267-8678; Monday – Friday, 8am – 10pm EDT.

We are also aware that there is confusion about the new Clozapine REMS Program requirements. Clozapine manufacturers are working to answer these questions and have posted additional information that is available by clicking on the "**Important Program Update**" button on the Clozapine REMS website (http://www.clozapinerems.com/) (http://www.fda.gov/about-fda/website-policies/website-disclaimer) homepage.

If you have questions or concerns about the Clozapine REMS Program or its website please contact FDA at druginfo@fda.hhs.gov (mailto:druginfo@fda.hhs.gov), 1-855-543-3784 or 301-796-3400.

Related Information

- FDA Drug Safety Communication: FDA modifies monitoring for neutropenia associated with schizophrenia medicine clozapine; approves new shared REMS program for all clozapine medicines (/drugs/drug-safety-and-availability/fda-drug-safety-communication-fda-modifies-monitoring-neutropenia-associated-schizophrenia-medicine)

Was this helpful? Yes No