

BACKGROUND AND CONTEXT

On October 12, 2015, the single shared Clozapine REMS Program was approved by FDA for ALL clozapine products, replacing all other clozapine patient registries.

At the time of launch, several key changes were made to how a prescription is filled, neutropenia monitoring recommendations and the treatment guidelines in clozapine prescribing information:

- **Absolute neutrophil count (ANC) is used exclusively for patient monitoring.**
 - ▶ White blood cell (WBC) counts are no longer accepted.
- **Patients with Benign Ethnic Neutropenia (BEN) can be treated with clozapine and have a separate ANC monitoring algorithm.**
- **ANC thresholds to continue clozapine treatment are lower.**
 - ▶ For **general population patients**, interrupt treatment if neutropenia is suspected to be clozapine-induced for **ANC less than 1000/ μ L**.
 - ▶ For **patients with BEN**, interrupt treatment if neutropenia is suspected to be clozapine-induced for **ANC less than 500/ μ L**.
- **Substantial drops in ANC do not require action unless the patient experiences neutropenia.**
- **Prescribers have greater flexibility to make patient-specific decisions** about continuing and resuming treatment in patients who experience moderate and severe neutropenia.
 - ▶ Patients **may be re-challenged** if the prescriber determines the risk of psychiatric illness is greater than the risk of severe neutropenia. In this case, a provider can enter a “treatment rationale” authorizing the patient to continue therapy.
- Prescribers and pharmacies must be specially certified in the new Clozapine REMS Program.
- Prescriptions from outpatient pharmacies will require what is called a “Pre-Dispense Authorization” or PDA from the REMS Program. Prescriptions from inpatient pharmacies require an eligibility check.

Given the significant changes being implemented, a transition period was put in place to allow pharmacists and prescribers to become certified in the program, enroll patients, and begin using the single shared system to manage patient care. In addition, pharmacies began conducting eligibility checks.

Based on feedback after program launch, the Clozapine REMS Program, in consultation with the FDA, extended the deadline for implementing the outpatient PDA. The goal was to minimize treatment disruption for patients while allowing more time for pharmacies and prescribers to complete certification.

NEXT STEPS

The Clozapine REMS Program will launch a limited version of the PDA in May of 2016. This will evaluate the criteria to authorize treatment, called program elements in the following manner:

INITIAL PDA LAUNCH: CLOZAPINE REMS PROGRAM ELEMENTS	PDA
Patient is registered Patient registration in the REMS will be evaluated. If a patient is not registered in the Clozapine REMS Program, this will prevent a PDA.	Not Issued
Patient ANC on file If patient does not have an ANC on file with the REMS, this will prevent a PDA.	Not Issued
Patient has low ANC <ul style="list-style-type: none"> • If the last ANC on file for a patient is a low ANC indicating moderate or severe neutropenia, it will prevent a PDA. • If the prescriber chooses to continue the patient on clozapine therapy, a treatment rationale must be provided to the Clozapine REMS Program from the prescriber before the dispense can be authorized; once the treatment rationale is submitted, proceed with obtaining a PDA. 	Not Issued <i>(if low ANC)</i> Issued <i>(if low ANC & treatment rationale submitted)</i>
Patient ANCs are current If last ANC draw date is outside of patient’s monitoring frequency (MF), it will not prevent a PDA (warning message will be displayed). <ul style="list-style-type: none"> • All PDA claim responses will provide the dispensing pharmacy with the last two ANC values and the associated blood draw dates, as well as the patient MF. • It is recommended that for patient safety reasons, pharmacies contact the prescriber to acquire the most recent patient ANC information and/or use clinical judgment before proceeding with dispense; more recent ANCs can be submitted by web, phone, or fax. 	Issued
Prescribers are certified Prescriber certification status will be evaluated but will not prevent a PDA (warning message will be displayed).	Issued
Pharmacies are certified Pharmacy certification status will be evaluated but will not prevent a PDA (warning message will be displayed).	Issued

This phased approach is designed to:

- Give prescribers and pharmacies more time to complete certification in the program.
- Allow prescribers and pharmacies more time to adjust to new prescribing information before the definition of a current ANC is strictly enforced.

When the full PDA launch occurs later in the year, if prescribers and/or pharmacies are not certified in the Clozapine REMS Program, or a patient’s ANC is not current, this will impact the pharmacy’s ability to dispense clozapine, negatively affecting patient care.



WHAT ARE MY RESPONSIBILITIES?

INITIAL PDA LAUNCH (MAY 2016)

FULL PDA LAUNCH (TARGET: Q4 2016)

WHAT IS CHANGING?	PRESCRIBERS	CHAIN PHARMACIES	INDEPENDENT OUTPATIENT PHARMACIES USING PHARMACY MANAGEMENT SYSTEM TO OBTAIN A PDA	INDEPENDENT OUTPATIENT PHARMACIES USING WEBSITE OR CALL CENTER TO OBTAIN A PDA	INPATIENT PHARMACIES
<ul style="list-style-type: none"> The initial Pre-Dispense Authorization (PDA) will be implemented in the outpatient environment. Eligibility check will continue in the inpatient environment. Initial PDA and eligibility check messaging will include indication of whether the prescriber and pharmacy are certified, although certification is not required at this time for a PDA to be issued. The initial PDA and eligibility check process will evaluate whether there is a ANC on file with acceptable values per the prescribing information or a treatment rationale on file documenting the prescriber's decision that the benefits outweigh the risks of dispensing clozapine. Initial PDA and eligibility check messaging will include the last two ANC values on file and their draw dates, as well as the patient's monitoring frequency (MF), although a current ANC is not required at this time for a PDA to be issued. Example: Last 2 ANC: 5100 01/12/16; 5300 12/18/15; MF=28d Because the initial PDA and eligibility check process will not evaluate whether the ANC on file is current relative to the patient's MF, pharmacies are expected to continue using their clinical judgment to determine if a more current ANC is necessary to dispense clozapine. 	<ul style="list-style-type: none"> Certify in program (one-time requirement) Ensure patients have current ANCs on file with the Clozapine REMS Program Use clinical judgment to determine if benefits of clozapine outweigh risks if a patient has an ANC indicating moderate or severe neutropenia; document this judgment with the Clozapine REMS Program as a treatment rationale 	<ul style="list-style-type: none"> Use pharmacy management system to obtain a PDA prior to dispense of clozapine Review ANC data (values and date of draw) provided with PDA and use clinical judgment to determine whether clozapine should be dispensed Work with chain authorized representative to certify in program (one-time requirement) <p>IF THE PDA IS DENIED</p> <ul style="list-style-type: none"> Work with patient and prescriber to get a current and acceptable ANC on file with the Clozapine REMS Program Work with prescriber to determine if a treatment rationale should be entered by the prescriber if a ANC is not within acceptable range per the prescribing information Work with prescriber to get patient enrolled in the Clozapine REMS Program 	<ul style="list-style-type: none"> Use pharmacy management system to obtain a PDA prior to dispense of clozapine Review ANC data (values and date of draw) provided with PDA and use clinical judgment to determine whether clozapine should be dispensed Certify in program (one-time requirement) 	<ul style="list-style-type: none"> Use Clozapine REMS Program website at clozapinerems.com or call center at 844-267-8678 to obtain a PDA prior to dispense of clozapine Review ANC data (values and date of draw) provided with PDA and use clinical judgment to determine whether clozapine should be dispensed Certify in program (one-time requirement) 	<ul style="list-style-type: none"> Use Clozapine REMS Program website at clozapinerems.com or call center at 844-267-8678 to conduct an eligibility check for a patient via Web or Contact Center before dispensing for the first time Certify in program (one-time requirement) <p>IF THE ELIGIBILITY CHECK IS NOT SUCCESSFUL</p> <ul style="list-style-type: none"> Work with patient and prescriber to get an ANC on file Work with prescriber to determine if a treatment rationale should be entered by the prescriber in the case of an ANC that is not within acceptable range per the prescribing information Work with prescriber to get patient enrolled in the Clozapine REMS Program
<p>When the PDA is fully launched, all of the Clozapine REMS program elements will be enforced as detailed below:</p> <ul style="list-style-type: none"> Prescribers and pharmacies are required to be certified to prescribe and dispense clozapine. The full PDA process will evaluate whether there is a ANC on file with acceptable values per the prescribing information or a treatment rationale on file documenting the prescriber's decision that the benefits outweigh the risks of dispensing clozapine. The full PDA process will evaluate whether the ANC on file is current relative to the patient's MF. <p>If any of the above conditions are not met, dispense of clozapine will not be authorized.</p>	<ul style="list-style-type: none"> Certify in program if not already certified (one-time requirement) Ensure patients have current ANCs on file with the Clozapine REMS Program Use clinical judgment to determine if benefits of clozapine outweigh risks if a patient has an ANC indicating moderate or severe neutropenia; document this judgment with the Clozapine REMS Program as a treatment rationale 	<ul style="list-style-type: none"> Use pharmacy management system to obtain a PDA prior to dispense of clozapine Work with chain authorized representative to certify in program if not already certified (one-time requirement) <p>IF THE PDA IS DENIED</p> <ul style="list-style-type: none"> Work with patient and prescriber to get a current and acceptable ANC on file with the Clozapine REMS Program Work with prescriber to determine if a treatment rationale should be entered by the prescriber if an ANC is not within acceptable range per the prescribing information Contact prescriber to certify if they have not done so Certify in the program if you have not done so Work with prescriber to get patient enrolled in the Clozapine REMS Program 	<ul style="list-style-type: none"> Use pharmacy management system to obtain a PDA prior to dispense of clozapine Certify in program if not already certified (one-time requirement) 	<ul style="list-style-type: none"> Use Clozapine REMS Program website at clozapinerems.com or call center at 844-267-8678 to obtain a PDA prior to dispense of clozapine Certify in program if not already certified (one-time requirement) 	<ul style="list-style-type: none"> Conduct an eligibility check for a patient via Web or Contact Center Certify in program if not already certified (one-time requirement) <p>IF THE ELIGIBILITY CHECK IS NOT SUCCESSFUL</p> <ul style="list-style-type: none"> Work with patient and prescriber to get an ANC on file Work with prescriber to determine if a treatment rationale should be entered by the prescriber in the case of an ANC that is not within acceptable range per the prescribing information Work with prescriber to get patient enrolled in the Clozapine REMS Program