Phone: 844-267-8678
Fax: 844-404-8876
www.clozapinerems.com

Dear Pharmacy Authorized Representative:

In late 2015, the Clozapine REMS Program, in consultation with the FDA, extended the deadline for implementing the Pre-Dispense Authorization (PDA). The goal was to minimize treatment disruption for patients while allowing more time for pharmacies and prescribers to complete certification. At that time, the Clozapine REMS Program indicated additional communication would be provided when additional information is available.

This letter is intended to describe the changes that will happen with the initial Pre-Dispense Authorization (PDA) launch in May 2016. The initial PDA launch evaluates some of the program elements that the Clozapine REMS Program has defined, and provides an authorization for the pharmacist to dispense accordingly.

As part of a 2-phase implementation, the initial PDA launch will provide warning messages if a prescriber and/or a pharmacy is not certified – but it will not prevent a dispense from being authorized. Similarly, if the most recent Absolute Neutrophil Count (ANC) is not current based on the patient's Monitoring Frequency (MF), this will not prevent a dispense from being authorized.

Note: 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.

Pharmacy authorized representatives that adjudicate claims electronically (i.e., "the switch") need to:

1. **Read this letter and understand the upcoming initial PDA launch and how it will affect all their outpatient pharmacy dispensing locations**
2. **Ensure that all outpatient pharmacy dispensing locations within their organization are trained and educated on the PDA**
3. **Ensure that all pharmacists in their organization understand the PDA messages and know how to use them to support dispense decisions**

Initial PDA Launch Plan

The Clozapine REMS Program is targeting the initial PDA launch (inclusive of the switch) for May 2016. The initial PDA launch will evaluate the following program elements for all clozapine prescription claims submitted through the switch.

Clozapine REMS Program Elements	PDA
Patient is registered • Patient registration in the REMS will be evaluated • If the patient is not registered in the REMS or not found in the REMS, a dispense will not be authorized and the claim will be rejected • The patient may be registered by the prescriber at www.clozapinerems.com or by phone at 844-267-8678 • The patient may be registered by the pharmacy via phone at 844-267-8678 during the transition period Note: Once the full PDA launch is implemented *later in the year,* patients must be registered by a prescriber or prescriber designee • Once the patient is registered and a current ANC is on file with the REMS, the claim may be re-submitted for dispense authorization • Sample reject message (actual message may vary): *"*REMS* - Patient not enrolled. Call 844-267-8678 for additional information and to enroll patient."*	**Patient Registered** ✓ Authorized **Patient not Registered** Dispense Not Authorized

The products covered under the Clozapine REMS Program are: Clozaril® (clozapine) tablets, for oral use • Versacloz® (clozapine, USP) oral suspension • Fazaclo® (clozapine USP) orally disintegrating tablets • Approved generic equivalents of these products

Clozapine REMS Program Elements	PDA

Patient Absolute Neutrophil Count (ANC) on file

- If a patient does not have an ANC on file with the REMS, a dispense will not be authorized and the claim will be rejected
- Patient ANCs may be submitted to the program at www.clozapinerems.com or by phone at 844-267-8678
- The ANC reporting form (available at www.clozapinerems.com) can also be used for submitting a patient ANC, however it will take up to 48 hours to process this form
- Once the patient ANC is submitted, the claim may be re-submitted for dispense authorization
- Sample reject message (actual message may vary): *"*REMS* - ANC results not on file. Contact prescriber"*

No ANC on File

Clozapine REMS Program Elements	PDA

Patient has low ANC

- If the last ANC on file for a patient is a low ANC indicating moderate or severe neutropenia, a dispense will not be authorized
- The pharmacy is requested to notify the prescriber of the low ANC
- If upon consult with the prescriber, the prescriber chooses to continue the patient on clozapine therapy, a treatment rationale must be provided to the REMS from the prescriber before the dispense can be authorized
- A prescriber may submit a treatment rationale at www.clozapinerems.com or by phone at 844-267-8678
- The ANC reporting form can also be used for submitting a treatment rationale, however it will take up to 48 hours to process this form.
- Once the treatment rationale is submitted, the claim may be re-submitted for dispense authorization

*Sample reject message (actual message may vary): *REMS* - ANC results out of range. Results Last 2 ANC: 400 01/12/16; 730 12/18/15; MF=7d*

Explanation of ANC Message

"Last 2 ANC"	The 2 most recent ANCs
"400 01/12/16"	Most recent ANC with value of 400 µL and a blood draw date of 01/12/16
"730 12/18/15"	Next most recent ANC with value of 730 µL and a blood draw date of 12/18/15
"MF=7d"	Patient has weekly Monitoring Frequency (MF) Other values:

"MF=14d"	Patient has bi-weekly Monitoring Frequency (MF)
"MF=28d"	Patient has monthly Monitoring Frequency (MF)
"MF=6m"	Patient has Monitoring Frequency (MF) of 6 months (Hospice)

Low ANC

Low ANC & Treatment Rationale On File

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Clozapine REMS Program Elements	PDA

Patient ANC is current

- All PDA claim responses will provide the dispensing pharmacy with the following information:
  - The 2 most recent ANC values and the associated blood draw dates
  - Patient Monitoring Frequency (MF)
- As long as the patient is registered, has an ANC on file, and the ANC is not low, a dispense will be authorized
- If the last ANC draw date is not current based on the patient's Monitoring Frequency (MF), this will not prevent a PDA
  - Note: Once the full PDA launch is implemented *later in the year,* patient ANCs must be current for a dispense to be authorized.
- While not required, it is recommended for patient safety that pharmacies contact the prescriber to acquire the most recent patient ANC information and/or use clinical judgment before proceeding with dispense
- If the pharmacy has or acquires an ANC that is more current than the last ANC draw date received back in the claim response, the pharmacy should submit the ANC to the Clozapine REMS Program
- Patient ANCs may be submitted to the program at www.clozapinerems.com or by phone at 844-267-8678. (The ANC reporting form can also be used for submitting a patient ANC, however it will take up to 48 hours to process this form.)
- If dispense does not occur, the pharmacy should reverse the claim
- Sample authorization message (actual message may vary):

*"*REMS* Rx authorized. Please evaluate latest ANC is current. Authorization Number ######## Last 2 ANC: 5100 01/12/16; 5300 12/18/15; MF=28d"*

Explanation of ANC Message

"Last 2 ANC"	The most recent 2 ANCs
"5100 01/12/16"	Most recent ANC with value of 5100 µL and a blood draw date of 01/12/16
"5300 12/18/15"	Next most recent ANC with value of 5300 µL and a blood draw date of 12/18/15
"MF=28d"	Patient has Monitoring Frequency (MF) of Monthly.

ANC is Current

✓ Authorized

Prescribers are certified

- Prescriber certification status will be evaluated; however, it will not prevent a dispense from being authorized
- If a prescriber is not certified in the system, a warning message will be displayed that the prescriber is not yet certified
- The warning message will contain content directing prescribers how to contact the Clozapine REMS Program to certify
- While not required, pharmacies may decide to contact prescribers regarding the need to certify soon
- Sample warning message (actual message may vary): *"*REMS* Rx authorized. Prescriber not currently certified. Prescriber can certify at www.clozapinerems.com or call 844-267-8678"*

Prescriber Certified

✓ Authorized

Prescriber not Certified

Authorized w/Warning

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Clozapine REMS Program Elements	PDA
Pharmacies are certified • Pharmacy certification status will be evaluated; however, it will not prevent a dispense from being authorized • If a pharmacy is not certified in the system, a warning message for the pharmacist will be displayed that the pharmacy is not yet certified • The warning message will contain content that directs pharmacies to certify. If a pharmacy dispense location receives this message, they must work with their authorized representative to complete training and necessary steps for enrollment • Sample warning message (actual message may vary): *"*REMS* Rx auth'd, but pharmacy not enrolled. Chain Pharmacies contact HQ Auth Rep. Others call your Help Desk or enroll at www.clozapinerems.com or call 844-267-8678"*	**Pharmacy Certified**  **Pharmacy not Certified**  **Authorized w/Warning**

After the initial PDA launch, data will continue to be evaluated. Should data demonstrate the need to modify the above criteria, pharmacies will be contacted accordingly.

For additional information related to the Clozapine REMS Program or the REMS Pharmacy Network, please contact the Clozapine REMS Program Contact Center at 844-267-8678.

Sincerely,

The Clozapine REMS Program

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