March Pharmacy Newsletter

The Food and Drug Administration (FDA) Announces Elimination of Clozapine REMS Program

The FDA has decided to discontinue the clozapine REMS program, meaning doctors, pharmacies, and patients are no longer required to participate in the mandatory reporting of absolute neutrophil count (ANC) blood test results before dispensing clozapine. The recommendation for prescribers is to monitor patients' ANC according to the monitoring frequencies described in the prescribing information. Information about severe neutropenia will remain in the prescribing information for all clozapine medicines, including in the existing Boxed Warnings. The risk of severe neutropenia with clozapine still exists, however, FDA has determined that the REMS program for clozapine is no longer necessary to ensure the benefits of the medicine outweigh that risk. The elimination of the REMS program is expected to decrease the burden on the health care delivery system and improve access to clozapine.

Clozapine is a second-generation antipsychotic medication prescribed for individuals with treatment-resistant schizophrenia, which means symptoms are not effectively managed by standard antipsychotics; it is particularly used when patients experience severe symptoms like hallucinations, delusions, and suicidal thoughts, which are characteristic of schizophrenia or schizoaffective disorder. Clozapine has a unique set of adverse side effects (i.e.: agranulocytosis, myocarditis, cardiomyopathy, and seizures) this necessitates close patient monitoring. Underutilization and delayed initiation of clozapine could have been due to fears surrounding prescribing clozapine, lack of familiarity with its use and the reporting requirements of the REMS program.

Key monitoring parameters for clozapine white blood cell count and absolute neutrophil count (ANC) is crucial, especially during the initial weeks of treatment when the risk of agranulocytosis is highest. Initiation of treatment include baseline assessment for abnormal movement disorder using scales such as Abnormal Involuntary Movement Scale (AIMS) or Dyskinesia Identification System: Condensed User Scale (DISCUS) rating assessment. Collecting baseline measurements of blood glucose, blood pressure, CBC with differential, heart rate, liver function tests, neurologic function, pregnancy testing for females, serum creatinine, serum electrolytes, serum lipid profile, serum prolactin, thyroid function tests (TFTs) and weight.

Noteworthy Interactions and Precautions

Concurrent use of other drugs known to cause neutropenia (i.e.: antineoplastic agents) increases the risk or severity of clozapine-induced neutropenia, consider increased absolute neutrophil count (ANC) monitoring and consult treating oncologist with concomitant use.

Concomitant use of amiodarone and clozapine increases the risk of QT/QTc prolongation and torsade de pointes (TdP) and may increase clozapine exposure and the risk for clozapine-related adverse effects. Consider a clozapine dose reduction and take steps to minimize the risk for QT/QTc interval prolongation and TdP, such as electrolyte monitoring and repletion and ECG monitoring, if concomitant use is necessary.

Avoid co-prescribing clozapine with other anticholinergic medicines that can cause gastrointestinal hypomotility, due to a potential to increase serious constipation, ileus, and other potentially serious bowel conditions that may result in hospitalization. Clozapine exhibits potent anticholinergic effects.

Avoid coadministration of azithromycin with clozapine due to the increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances.

Tobacco smoking may increase the clearance of clozapine, resulting in reduced plasma concentrations and the potential loss of efficacy. Tobacco smokers may require higher clozapine doses.

Oral disintegrating clozapine tablets (i.e.: FazaClo) may contain aspartame and should be used cautiously in patients with phenylketonuria. Phenylalanine is a component of aspartame. Each 25 mg orally disintegrating tablet of FazaClo contains 3.1 mg of aspartame (1.74 mg of phenylalanine), and each 100 mg oral disintegrating tablet of FazaClo contains 12.4 mg of aspartame (6.96 mg of phenylalanine).

Please note these interactions and precautions are not a complete list, however, awareness of these components is essential for enhancing patient safety. Effective monitoring helps to avoid serious medication-related issues.

References:

1. https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/frequently-asked-questions-clozapine-rems-modification
2. https://www.clinicalkey.com/pharmacology/monograph/142?n=cloZAPine
3. https://www.micromedexsolutions.com/micromedex2/librarian/CS/317727/ND_PR/evidencexpert/ND_P/evidencexpert/DUPLICATIONSHIELDSYNC/82589E/ND_PG/evidencexpert/ND_B/evidencexpert/ND_AppProduct/evidencexpert/ND_T/evidencexpert/PFActionId/evidencexpert.DoIntegratedSearch?SearchTerm=clozapine&UserSearchTerm=clozapine&SearchFilter=filterNone&navitem=searchGlobal#

PREFERRED DRUG LIST UPDATES CAN BE FOUND HERE:

ACC-RBHA, DD, ALTCS and DCS CHP	Behavioral Health (Non-Title 19/21)

** Drugs that are not on the formulary will require a PA (prior authorization) request to be submitted**

Reminder for quicker determinations of a Prior Authorization use the ePA link for Our Providers: Please click here to initiate an electronic prior authorization (ePA) request.

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