February, 14 2022

Patrizia Cavazzoni, M.D.
Director
Center for Drug Evaluation and Research
U.S. Food and Drug Administration
10903 New Hampshire Ave
Silver Spring, MD 20993-0002

Dear Dr. Cavazzoni,

On behalf of the undersigned organizations, we would like to urge the Food and Drug Administration (FDA) to continue the temporary suspension and provide an update on the Clozapine Risk Evaluation and Mitigation Strategies (REMS) implementation. Specifically, on November 19, we were informed that the suspension of certain provision of the REMS program for clozapine would continue 90 days or until the issues were resolved. We do not feel the issues are resolved and want to be assured that this suspension will continue past February 17, 2022. Furthermore, we want to be assured that we will receive at least a 60-day notice if the suspension is to be ended.

In addition, during listening sessions held on December 2 and December 16, we raised specific concerns that impact patients' continuity of care. These issues must be addressed given the potentially fatal outcomes patients may experience if Clozapine is suddenly stopped. In fact, the Institute for Safe Medication Practices published a report in the January 13, 2022, issue of their Acute Care newsletter detailing such a case. A patient who had been stable on Clozapine was taken off the drug due to their psychiatrist's inability to enroll in the New Clozapine REMS. As you may be aware, the patient was subsequently hospitalized, restarted on Clozapine and experienced a cardiac arrest shortly after receiving their restart dose. It is unacceptable for a REMS with unproven effectiveness at meeting its goal to carry risks of interruptions that can result in rehospitalization, acute exacerbation of psychosis, increased risk of suicide and potentially fatal orthostatic hypotension/bradycardic syndromes associated with incorrect restarts. We feel certain that this case reported in the literature is not the only serious adverse outcome from the REMS and the transition.

While we anticipated adverse outcomes like the one reported above, the lack of a test period for the new REMS makes us fearful of additional unanticipated consequences such as those that occurred on the implementation of the new REMS. Given the grave concerns of the stakeholders and these severe risks that the REMS poses to patients, we request a response to the following questions:

1. Does FDA intend to continue to allow pharmacies to order clozapine from wholesalers without restriction?
2. Does the FDA intend to allow pharmacies to dispense clozapine without a REMS Dispensing Authorization?
3. Does the FDA intend to allow hospitals to dispense clozapine without obtaining a REMS Dispensing Authorization every time the drug is dispensed?
4. Does the FDA or Clozapine Products Manufacturing Group (CPMG)/Clozapine REMS intend to address the limitation on discharge supplies of clozapine from acute care hospitals?
5. Does the FDA or CPMG/Clozapine REMS intend to revise the definitions of pharmacy types in the REMS to address concerns about workload and workflow for psychiatric facilities/hospitals?

6. Does the FDA or CPMG/Clozapine REMS intend to address the issue concerning individuals not being able to fulfill multiple roles with a single email address? This includes prescribers covering for other prescribers as designees and pharmacists acting as pharmacists and prescribers or pharmacists acting as pharmacists and designees?
7. Does the FDA or CPMG/Clozapine REMS intend to enter into a dialogue to discuss patient status form (PSF) workflow?
8. Does the FDA or CPMG/Clozapine REMS intend to implement a process through which prescribers can review historical absolute neutrophil count (ANC) data for their patients?
9. Does the FDA intend to reconsider the need for the Clozapine REMS and/or discuss this matter in a public forum such as a meeting of the Psychopharmacologic Drugs Advisory Committee?

Please let us know if you would like to set up a meeting to discuss these issues. Again, we request an update and a reasonable notification period prior to the temporary suspension ending. If the suspension ends, we are concerned the same issues will be experienced as when the REMS was first launched.

Sincerely,

American Association For Community Psychiatry

American Psychiatric Association

American Psychiatric Nurses Association

College of Psychiatric and Neurologic Pharmacists

National Alliance on Mental Illness

National Association of State Mental Health Program Directors

National Council for Mental Wellbeing

CC: Rachel Levine, M.D., Assistant Secretary for Health, Department of Health and Human Services

Miriam Delphin-Rittmon, Ph.D. Assistant Secretary for Mental Health and Substance Use, Department of Health and Human Services

Cynthia LaCivita, Pharm. D., Director, Division of Risk Management, Food and Drug Administration

Claudia Manzo, Pharm. D., Director, Office of Medication Error Prevention and Risk Management, Food and Drug Administration