|  |  |  |  |
| --- | --- | --- | --- |
| |  |  |  | | --- | --- | --- | | |  |  | | --- | --- | | |  | | --- | | **Clozapine REMS A Barrier To Treatment And Unnecessary For Safe Use, US FDA Adcomms Say**  20 Nov 2024 • By [Sue Sutter](https://oaqlbb.clicks.mlsend.com/tl/c/eyJ2Ijoie1wiYVwiOjU0NDUxMixcImxcIjoxMzg0OTU5ODU3NzE4NzM4NjksXCJyXCI6MTM4NDk1OTk2MDE3NTA5ODcwfSIsInMiOiJhNGFhYjMxMDFjYjFkMGU0In0)  The atypical antipsychotic’s Risk Evaluation and Mitigation Strategy should be retired because the requirements for prescriber education and documentation on absolute neutrophil count monitoring are hindering access, panelists said.  Many open public hearing speakers at the advisory committee meeting wore t-shirts attesting to clozapine's safety. (Sue Sutter)  **Key Takeaways**   * **Two advisory committees voted that the clozapine REMS’ education and documentation requirements were not necessary for the antipsychotic’s safe use.** * **The REMS should be retired because it is a barrier to access for the drug, which is a highly effective for treatment-resistant schizophrenia, panelists said.** * **More than 25 patients, family members and health care providers spoke during the open public hearing about the challenges of accessing clozapine and the consequences when treatment is interrupted due to documentation deficiencies in the REMS.**   The clozapine Risk Evaluation and Mitigation Strategy appears headed for elimination after two US Food and Drug Administration advisory committees voted that the program’s education and documentation requirements were not necessary for the antipsychotic’s safe use.  Members of the drug safety/risk management and psychopharmacologic drugs panels voted 14-1 on 19 November that the REMS requirement for prescribers to document absolute neutrophil count (ANC) results and for the pharmacy to verify those results were unnecessary.  The joint panel similarly voted 14-1 that the REMS requirement for health care providers to learn about the risk of severe neutropenia and the need for ANC monitoring was not necessary.  Panelists said clozapine is a highly effective, but underutilized antipsychotic for treatment-resistant schizophrenia and the drug’s benefits outweigh the risk of severe neutropenia for the vast majority of patients.  Although the REMS was well intentioned, it has presented numerous obstacles to prescribing and effective use, committee members said.  “It’s time to retire the clozapine REMS,” said panelist Jess Fiederowicz, chief of mental health at Ottawa Hospital, who participated virtually.  “I strongly feel that the REMS at this point is just a hindrance,” said Rajesh Narendran, psychiatrist at UPMC Western Psychiatric Hospital. “I think you should get rid of the REMS.”  Prescribers should be trusted to read the drug’s label and follow the recommendations for regular ANC monitoring rather than be bound by the documentation requirements of a REMS, Narendran said.  “The amount of benefit that can come from clozapine is so great that any mandatory monitoring” of ANC levels under a REMS for “any amount of time, I feel, would be dangerous,” said Gopal Vyas, clinical assistant professor at the University of Maryland Department of Psychiatry.  Panelists also said there was sufficient information about the risk of severe neutropenia with clozapine and the need to conduct blood testing available outside the REMS that the prescriber education requirement was no longer necessary.  **Enforcement Discretion Not Well Understood**  The clozapine REMS requires prescriber education and certification, pharmacy certification and patient enrollment. Prescribers must obtain baseline ANC results for a patient and monitor ANC levels at regular intervals during treatment. Documentation of blood testing results through the REMS allows the patient to receive clozapine.  The REMS has undergone several modifications and has never been fully enforced due to technical and operational challenges and concerns about interrupting patient access to the drug. The FDA exercised its [enforcement discretion](https://oaqlbb.clicks.mlsend.com/tl/c/eyJ2Ijoie1wiYVwiOjU0NDUxMixcImxcIjoxMzg0OTU5ODU3NzUwMTk1OTgsXCJyXCI6MTM4NDk1OTk2MDE3NTA5ODcwfSIsInMiOiI5YWU2YWRjZmMwMDYzODljIn0), meaning that patients, prescribers and pharmacies are able to access clozapine outside of the REMS.  However, the enforcement discretion is not well understood by all stakeholders in the health care ecosystem. Some pharmacies insist they cannot fill a prescription without documentation of ANC results.  Some advisory committee members were not familiar with the enforcement discretion policy. Others said the term itself has created adverse consequences in the real world, with prescribers and pharmacists afraid to prescribe or dispense the drug outside the REMS requirements for fear they will lose their license or be sued.  Walter Dunn, director of the Mood Disorders Section at West Los Angeles Veterans Affairs Medical Center, was the lone panelist to support keeping some REMS restrictions. He favored a REMS requirement for monitoring during the first 18 weeks of therapy, when the risk of severe neutropenia is highest, but with a more streamlined risk management program that does not require documentation of ANC levels.  Dunn also questioned whether modifying or eliminating the REMS would result in more providers willing to prescribe the drug and more patients willing to take it.  **Boisterous Public Hearing**  The committee vote followed a boisterous open public hearing where more than 25 patients, family members and health care providers testified to the challenges of accessing clozapine and the consequences when treatment is interrupted due to documentation deficiencies in the REMS.  OPH speakers spoke of family members who committed suicide after their physicians were unwilling to prescribe clozapine because the requirements were too burdensome, or pharmacies were unwilling to dispense the drug.  **“The greatest risk of clozapine is not getting clozapine,”** OPH speakers said.  “The greatest risk of clozapine is not getting clozapine,” was a common refrain among OPH speakers.  Several speakers also testified to the challenges drawing blood from schizophrenic patient, and the “no blood, no drug” philosophy of pharmacies that continue to require ANC documentation despite the FDA’s enforcement discretion for the REMS.  In a highly unusual move, the mother of the advisory committee’s patient representative, Michael Brisbin, testified about her son’s challenges obtaining clozapine. Another mother showed a picture of her son, who died by suicide, in a coffin.  Many OPH speakers and audience members wore black t-shirts bearing the slogan “Clozapine is the safest antipsychotic in the world.” They clapped and cheered throughout the meeting, but sometimes objected to statements from the FDA and industry representatives.  As the meeting ended, Tiffancy Farchione, director of the FDA’s Division of Psychiatry, assured the audience that the agency heard the testimony of patients and caregivers.  “What you shared today will have an impact on regulatory decision-making,” she said. | | | |