Congress of the United States

Washington, DC 20515

August 9, 2023

The Honorable Robert M. Califf, M.D.
Commissioner
U.S. Food and Drug Administration
White Oak Building One
10903 New Hampshire Ave.
Silver Spring, MD 20993

Dear Commissioner Califf:

We are writing to express our deep concern about the application of your agency's Risk Evaluation and Mitigation Strategy (REMS) drug safety program to the antipsychotic medication clozapine. There is an emerging body of well-documented scientific evidence that the REMS process is operating as a barrier to the use of this life-saving medication – and is causing physical harm to the people who need it most. We urge you to undertake immediate reforms.

Clozapine is the only FDA-approved atypical antipsychotic medication for treatment-resistant schizophrenia. The advantages of this therapy include lowering the risk of suicide, reduced risk of movement disorders (tardive dyskinesia and extrapyramidal effects) and fewer relapses. Clozapine also has been shown to reduce suicidal behavior even in people with non-treatment-resistant schizophrenia and schizoaffective disorder.

It is startling to note that fully 50% of the more than 2.8 million people in the United States living with schizophrenia have a treatment-resistant form of this severe brain disease. Clinical data demonstrate that this patient population experiences extraordinarily high rates of mortality and morbidity. Lack of available treatments or inability to access them due to administrative barriers (especially clozapine) results in these patients being disproportionately and inappropriately warehoused in homeless shelters, county jails and community hospital emergency departments.

Given these circumstances, the FDA must undertake urgent reforms of the REMS program for clozapine. Specifically, the REMS requires frequent hematologic monitoring and reporting. Although well intended, the REMS is now operating as an active barrier to clozapine use by causing widespread confusion among pharmacists and prescribing physicians who are seeking to provide their patients with the clinical benefits of clozapine while struggling to adhere to the hematologic monitoring mandates.

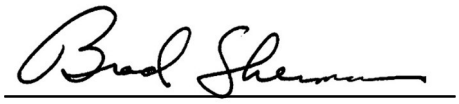
If patients taking clozapine miss even one blood draw – or the REMS computer system doesn't accurately record the result of a test – patients are denied their medication refills. Within just a few days of this treatment denial, patients can suffer severe psychosis that erases previous treatment progress. Some commit suicide.

In addition, recent search shows that African Americans are especially disadvantaged by the clozapine REMS. Because Black people may have lower normal white blood cell counts (benign ethnic neutropenia), these patients are inaccurately subject to the FDA's increased documentation and hematologic monitoring because of confusion about what benign ethnic neutropenia is. In fact, the REMS suggests that lower but normal white blood cell counts in Black patients are a "condition," despite most African American patients (68%) being genetically predisposed to run lower. The result of this confusion is reduced access to potentially lifesaving medication.

The overwhelming scientific evidence suggests that the burdens imposed by the clozapine REMS program substantially outweigh the risk posed by the medication's potential side effects. Therefore, we strongly urge the FDA to reduce clozapine-related barriers by shifting its REMS program to one with an educationally oriented focus for prescribers, pharmacists and front-line clinicians.

Thank you for your attention to this important and urgent matter.

Sincerely,



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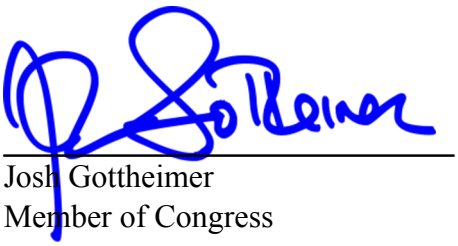

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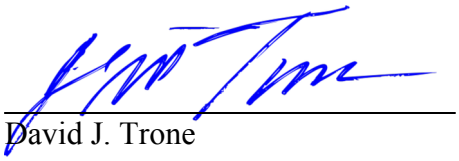

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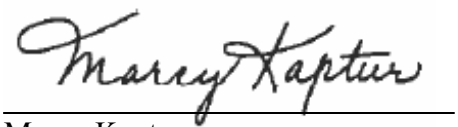

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