



**Schizophrenia
& Psychosis**
Action Alliance

The Clozapine REMS: Eliminating a Barrier to Lifesaving Care

Deanna L. Kelly, PharmD, BCPP

MPower Professor of Psychiatry, *MPowering the State*

Acting Director, Maryland Psychiatric Research Center

Chief, Treatment Research Program, University of Maryland School of Medicine

Director of the clozapine CHAMPION project & Statewide Consultation Line

American Psychiatric Association SMI Advisor Expert

American Association of Psychiatric Pharmacists (AAPP) Past President

Dr. Deanna Kelly – Credentials & Expertise

- **25 years of research and clinical experience with schizophrenia and clozapine**
- Director of an inpatient schizophrenia research unit
- APA SMI Advisor, clozapine expertise and tip developer
- SAMHSA Clozapine Advisory Committee
- FDA Advisory committees
- International clozapine publications and guidelines
- Led statewide educational intervention program on clozapine
- Director of the State of Maryland clozapine consultation line
- Published over 230 publications (over 25% on clozapine)
- Published books and book chapters on schizophrenia and clozapine
- 30+ grants in schizophrenia, including 10 NIH grants

Schizophrenia

- Today is **World Schizophrenia Day**
- Schizophrenia* is a chronic **brain disorder** that affects about 1.6% of the U.S. population
 - **~5.6 million individuals**
- Delusions, hallucinations, disorganized speech, thought and movement disorders
- **Important:** Schizophrenia is **treatable** with medications

Challenges of schizophrenia care

- Top 15 leading causes of disability worldwide
- Schizophrenia lifespan is cut short by more than 25 years
- 5% die by suicide
- 50% attempt suicide
- Very high financial burden of undertreated schizophrenia:
 - **\$281.6 billion** annually (direct and indirect costs)

Treatment pitfalls

- Up to 50% of a people with schizophrenia have Treatment-Resistant Schizophrenia (TRS)
- **CLOZAPINE:**
 - The **ONLY** FDA-approved medication for TRS
 - The **ONLY** FDA-approved medication to reduce suicide
- Up to 2.8 million people in U.S. with TRS
- In US used in less than 5% of all patients

A major problem

Clozapine saves lives and lowers costs

Clozapine is severely underused!

WHY?

A major barrier: Frequent Blood Tests

- **Mandatory** laboratory blood tests for ALL clozapine patients:
 - **WEEKLY** draw for “neutrophil counts” (ANC) *for 6 months*
 - Biweekly ANC for *months 6 through 12*
 - Monthly ANC after 1 year – **INDEFINITE**
- **History:** In 1975, 8 patients in same area of Finland died from “severe neutropenia”
 - Clozapine was pulled from the US drug market
 - The FDA allowed clozapine to be returned in 1990 with conditions:
 - Frequent blood testing of “ANC” to detect severe neutropenia
 - A surveillance program to monitor the testing



**Schizophrenia
& Psychosis**
Action Alliance



Overview of Risk Evaluation and Mitigation Strategies (REMS)

Frequent Blood Tests: How?

- **Risk Evaluation and Mitigation Strategy (REMS)**
 - Intended as safety program
 - FDA establishes need for program
 - This particular REMS is referred to as “**The clozapine REMS**”
 - A surveillance platform to monitor the blood test results (ANC)
 - A cumbersome system that requires certification of prescriber and pharmacy, submit blood results, pharmacy authorization, etc.
 - **Patients must participate to receive clozapine**
 - Errors, missing data, and missed bloodwork prevent clozapine dispensing
 - Prescribers have some discretionary ability but often pharmacies don't
- **The current clozapine REMS compounds the underuse problem...**
 - **It does not improve clozapine prescribing!**

Because of the clozapine REMS:

- Many prescribers will not enroll in the system
- Patients have not been able to find doctors willing to prescribe clozapine
- Patients cannot find pharmacies willing to dispense clozapine
- Healthcare providers experience a high burden & little benefit from the REMS
- Treatment has been disrupted
- Some patients have relapsed, some hospitalized, some injured... even deaths
- Some patients have not returned to previous levels of functioning
- Utilization of clozapine has not improved – it may be even lower

**Lack of studies showing benefit after
30 years of blood tests and 8 years of the clozapineREMS**

Mental Health Community Consensus

No available evidence the REMS prevents more harm than it causes

OR

Reduce Scope of Clozapine REMS

- Eliminate mandatory reported blood tests
 - Eliminate pharmacy authorizations
 - Improve provider education

The Clozapine REMS Should Be Eliminated



**Schizophrenia
& Psychosis**
Action Alliance

American Association
of Psychiatric Pharmacists



Improving minds. Improving lives.

Pressure from All Fronts

Professional associations speak out

FDA Listening Session, Feb. 1, 2023:

Proposed elimination of REMS or change to education-based program



Leading provider associations represented 54,000 members

Largest U.S. mental health advocacy organizations also participated

Patients and families speak out

- Families complain to NAMI:
 - Can't find doctors willing to prescribe clozapine
 - Pharmacy & lab errors, miscommunication
 - Lifelong requirements for blood testing
 - Years of unnecessary suffering, suicide, near-death events due to ineffective treatment instead of clozapine
 - Families have to “stockpile” clozapine to avoid interruptions



Patients and families speak out

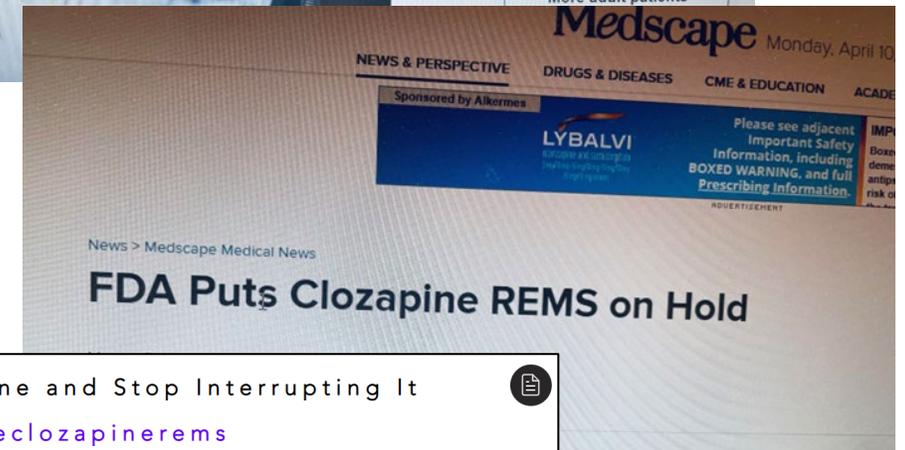
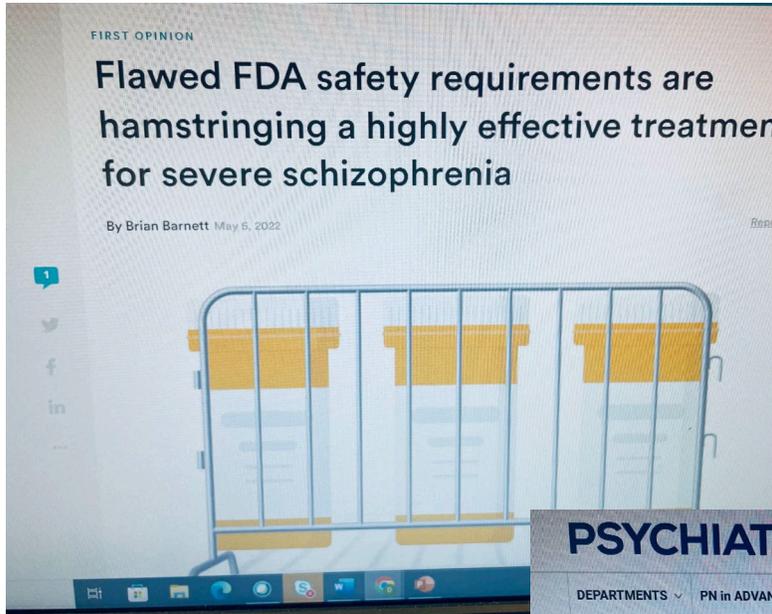
- S&PAA's Patient-Focused Drug-Development meeting on schizophrenia (Nov 2022).

“Please, stop making it so hard to get a lifesaving medication. My daughter has had a meaningful recovery because of clozapine!”

“One family resorted to buying clozapine from Mexico.”

“REMS has now robbed us of our wonderful psychiatrist.”

Media speak out



#EndtheClozapineREMS



Start Using Clozapine and Stop Interrupting It
#endtheclozapinereMS

The Angry Moms

Join the Army of Angry Moms | Media Inquiries / Request Info | Report a Problem Obtaining Clozapine

Original architect speaks out

- **Dr. Gilbert Honigfeld**

- 50 years of experience
- Oldest surviving member of U.S. medical team that helped shepherd clozapine through regulatory review

The Clozapine REMS should be eliminated ASAP!

Even the original architect speaks out!

- **Dr. Honigfeld's Letter to the FDA:**

- The clozapine REMS was intended to be short-lived
- Many other medications linked to severe neutropenia:
 - Yet, it's the ONLY medication with a REMS requiring blood tests!
- U.S. clozapine use is lower than any other country!
 - Finland's use is 10x higher

“After 30 years of post-market experience, psychiatrists are well informed on hematologic risk”

Clinicians speak out

- **Clozapine CHAMPION program:**
 - Clozapine education program and consultation hotline in the State of Maryland
 - Created to improve access to clozapine and help providers improve use
- **Most common call: Requesting help with the clozapine REMS**
 - 40% more calls come in seeking help with REMS than for all other issues of severe side effects, adjunct treatment or off-label use
 - Many prescribers continue to avoid clozapine REMS registration
- **Challenges finding outpatient prescribers once out of hospital**

More people have confusion, issues and misunderstandings about the clozapine REMS than with using the medication itself

Researchers speak out

- Growing body of published literature suggesting that clozapine REMS is problematic
- Presentation today in San Francisco at APA meeting showing focus groups identified numerous barriers and issues
- Collective CALL to ACTION in research community

Angry parents speak out

Kevin Keith Langemeier, 49, died in March 2023 in an officer-involved shooting in Texas while he was experiencing severe delusions

His relapse occurred soon after his clozapine prescription was interrupted

“His mother desperately tried to get his Clozapine restocked... However, despite Kevin running out of Clozapine on Wednesday, it wasn't filled until Monday. This was the day before his death. By that point, his mental disorder had taken control and his mother didn't have resources to calm him down and stabilize him.”

Three decades of science should speak the final word

- Little known published data available supports the safety of the clozapine REMS
- We now know:
 - Neutropenia is not as dangerous as previously thought (risk of death 0.05%)
 - The original concerns from the 1970s have not repeated
 - Blood draw logistics (i.e., REMS) is the No. 1 reason for underuse
 - Patients of African descent face worse discrimination
 - Suicide risk associated with not using clozapine is **MUCH HIGHER** than the 0.4% that develop severe neutropenia from clozapine
- Other countries have fewer clozapine restrictions:
 - They have higher clozapine use
 - Their rates of severe neutropenia are NOT higher
- Clozapine saves lives and prevents suicide

No known FDA data available suggests the clozapine REMS saves lives, reduces interruptions, or that patients benefit from testing

Conclusions

- Patients who need clozapine often can't access this vital treatment
- The risk of clozapine nonuse and consequences outweigh the low risk of death from severe neutropenia
- **ALL** key U.S. stakeholders are calling for ACTION:
 - Providers, parents, advocacy groups, experts, healthcare workers, mental health associations, researchers, pharmacy groups and the media
- After 30 years, it's time to revisit the rationale for stringent blood test oversight

**Patients with schizophrenia deserve access to the
ONLY medication FDA-approved for TRS and suicidal behavior:
opportunity for life saving care**



**Schizophrenia
& Psychosis**
Action Alliance

American Association
of Psychiatric Pharmacists



Improving minds. Improving lives.

Thank You