Errata to FDA Briefing Document

Risk Evaluation and Mitigation Strategy (REMS) for Clozapine Products
Joint Meeting of the Drug Safety and Risk Management Advisory Committee and the Psychopharmacologic Drugs Advisory Committee
November 19, 2024

This erratum contains corrections to FDA's Briefing Document for the November 19, 2024, Joint Meeting of the Drug Safety and Risk Management Advisory Committee and the Psychopharmacologic Drugs Advisory Committee. The committee will discuss the Risk Evaluation and Mitigation Strategy (REMS) for Clozapine.

1) Section 1.2, Page 9; and Section 7, page 58

"Data reported by the CPMG from the two most recent REMS assessment reports suggest that over 45,000 patients per year could have had their clozapine treatment withheld or delayed if all REMS safe use requirements were enforced."

Revised text (deletions in ~~strikethrough~~ and additions are **bolded and underlined**):

Data reported by the CPMG from the two most recent REMS assessment reports ~~suggest that over 45,000 patients per year could have had their clozapine treatment withheld or delayed if all REMS safe use requirements were enforced~~ **indicates that use of the transition and dispense rationales allowed 64,208 patients access to clozapine. Both of the dispense rationale options allowed for authorization of a clozapine dispense despite not all REMS safe use conditions being met and prevented interruptions or delays in clozapine treatment.**

2) Section 2.4.3, Page 25

"There are no limitations on the amount of clozapine that can be dispensed for outpatients; however, the Guide for Pharmacists recommends dispensing a days' supply consistent with the patient's monitoring frequency. At the time of discharge, an inpatient pharmacy is limited to dispensing a 7-day supply."

Revised text: (deletions in ~~strikethrough~~ and additions are **bolded and underlined**):

There are no limitations on the amount of clozapine that can be dispensed for outpatients; however, the Guide for Pharmacists recommends dispensing a days' supply consistent with the patient's monitoring frequency. **While the Clozapine REMS does not specifically limit days' supply in the outpatient setting, the REMS system includes an entry limit of 30 days' supply on each dispense when a pharmacy enters dispensing information into the REMS system.** At the time of discharge **from an inpatient setting**, an inpatient pharmacy is limited to dispensing a 7-day supply.

3) Section 3.2, Table 4, Page 29

Revised Table (deletions in ~~strikethrough~~ and additions are **bold and underlined**):

Table 1. Prescriber Knowledge Rates for Survey Knowledge Domains over Time

Assessment Report	Report 1	Report 3	Report 4	Report 7
Date received by FDA	2017	2020	2021	2024
Number of survey respondents	n=200	n=300	n=300	n=316
Survey knowledge domain	% Correct (95% CI)	% Correct (95% CI)	% Correct (95% CI)	% Correct (95% CI)
1. Understand the risk of severe neutropenia associated with clozapine	86% (not reported)	92% (not reported)	~~92%~~ **91%** (89-92)	93% (91-94)
2. Understand the need for appropriate patient monitoring with clozapine	79% (not reported)	86% (not reported)	82% (80-84)	93%* (91-94)

Source: Adapted by the FDA REMS assessment analyst from tables 32, 33, and 34 from REMS Assessment Report 1, tables 57, 58, and 59 from REMS Assessment Report 3, tables 61, 62, and 63 from REMS Assessment Report 4 **and Table 11 from Appendix 7 in REMS Assessment Report 4**, and tables 11, 12, and 13 from Appendix 13 of REMS Assessment Report 7.
*The questions used to measure Survey Knowledge Domain 2 changed for the 2024 survey, so results are not directly comparable to prior surveys.
Note: Surveys were not conducted every year.
Abbreviations: CI, confidence interval; FDA, U.S. Food and Drug Administration; n, number of survey respondents; REMS, Risk Evaluation and Mitigation Strategy

4) Section 3.3, Table 6, Page 30

Revised Table (deletions in ~~strikethrough~~ and additions are **bold and underlined**):

Table 2. Patient and Caregiver Knowledge Rates for Relevant Survey Questions Over Time

Assessment Report	Assessment Report 3	Assessment Report 4	Assessment Report 7
Date received by FDA	2020	2021	2024
Number of survey respondents	n=300	n=300	n=729
Survey question	% Correct (95% CI)	% Correct (95% CI)	% Correct (95% CI)
1. Which of the following can occur when taking clozapine? Clozapine can cause white blood cells, called neutrophils, to drop in number. This is called neutropenia.	67% (62 – 72)	72% (67 – 77)	~~76%~~ **75%** (72 – 79)
2. 75%Clozapine can cause certain white blood cells to drop, which could lead to which of the following: Serious infections and death	53% (47 – 59)	65% (59 – 70)	61% (57 – 64)
3. What are the requirements that a patient must complete to receive Clozapine?			
Have… blood tested before starting treatment with clozapine	87% (83 – 90)	87% (83 – 90)	88% (85 – 90)
During clozapine treatment, …have regular blood tests	97% (94 – 98)	97% (94 – 98)	97% (96 – 99)

Source: adapted by the FDA REMS assessment analyst from tables 86, 87, and 88 from REMS Assessment Report 3, tables 96, 97, and 98 from REMS Assessment Report 4, and tables 49, 50, and 51 from Appendix 13 of REMS Assessment Report 7.
Note: Surveys were not conducted every year; the survey waves for assessment reports 1 and 2 (conducted in 2017 and 2018) used different question wording so results are not presented.
Abbreviations: CI, confidence interval; FDA, U.S. Food and Drug Administration; n, number of survey respondents; REMS, Risk Evaluation and Mitigation Strategy