
To: Dockets Management Staff (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

From: American Association of Psychiatric Pharmacists

Subject: Docket No. FDA-2023-N-0573 for Changes to Third-Party Vendors for Risk Evaluation and Mitigation Strategies; Establishment of a Public Docket; Request for Comments

Date: July 7, 2023

On behalf of the American Association of Psychiatric Pharmacists (AAPP), we provide the following comments on FDA's Public Docket: Changes to Third-Party Vendors for Risk Evaluation and Mitigation Strategies (REMS). AAPP is a professional association of nearly 3,000 members who envision a world where all individuals living with mental illness, including substance use disorders, receive safe, appropriate, and effective treatment. Members are specialty pharmacists, and most are Board Certified Psychiatric Pharmacists (BCPPs) who specialize in psychiatry, substance use disorders (SUDs), and psychopharmacology. They graduate with a Doctor of Pharmacy degree, requiring six to eight years of higher education to complete, and have more training specific to medication use than any other health care professional.

Psychiatric pharmacists and their patients have experienced the detrimental effects of a change in REMS that did not benefit from stakeholder input. Specifically, changes in the vendor for the Clozapine REMS resulted in reduced access to the medication for patients, actual harm to patients, frustration for prescribers and pharmacists, increased workload for multiple health care providers and reduced use of this life saving medication. AAPP is on record questioning the need for elements to assure safe use (ETASU) for the clozapine REMS when evidence points to the fact that clozapine remains underused in the US and, in countries without monitoring there is no greater rate of severe neutropenia.

However, as requested, our comments are restricted to recommendations and comments regarding changes in vendors for an operating REMS program.

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## Stakeholder Input

*Stakeholder Diversity*
AAPP believes that physicians, pharmacists, nurse practitioners, nurses, and physician assistants should be invited to provide input into a change in the REMS. Patients and their advocates should also be invited to participate through appropriate advocacy organizations. Rather than seeking academics or other thought leaders, those providing input should be frontline health care providers who actually deal with the REMS and use the vendor's present system. This input should include national health care provider organizations as well as relevant specialty health care provider organizations (such as AAPP). Relevant state governmental input (such as the National Association of State Mental Health Program Directors – NASMHPD in the case of clozapine) should also be invited particularly for agents highly utilized in public health and behavioral health programs.

*Timing of Stakeholder Input*
Stakeholder input should begin at least one year before changeover if the REMS is complicated and/or contains numerous elements affecting multiple steps in the medication use process. For REMS containing relatively few elements, stakeholder input should be solicited at least six months prior to the changeover.

*Solicitation of Stakeholder Input*
In addition to contact with relevant stakeholder organizations as noted above, the current vendor should include a notice of intended change on its website and any communications with health care providers. Such a notice should contain an internet link to obtain details about the change and how to provide input in the process. Similarly, the manufacturer or manufacturer's group should provide the same notices. An electronic notice should be sent to each user of the current system as well as individuals who have provided past testimony or comments regarding the REMS to the FDA, manufacturer (or manufacturing group) and vendor.

## Testing of New REMS System

AAPP urges the FDA to require stakeholder testing of the new REMS. Testing would include a survey of test users to determine:

- Does any element or implementation of the new system pose additional challenges to prescribers, pharmacists, patients, wholesalers, health care administrators or health care sites?
- Is any element or provision of the new system more restrictive than the current system in the view of prescribers, pharmacists, patients, wholesalers, health care administrators or health care sites?
- Does the new system require a greater expenditure of resources than the current system?
- Will the new system require implementation costs for prescribers, pharmacists, patients, wholesalers, health care administrators or health care sites?
- Does the new system impact drug purchasing, approval of payment by PBMs and insurers, or other administrative systems?
- Is the new system at least as compatible with prescriber and pharmacy workflow and documentation than the current system?
- What alterations in the proposed system could improve access, reduce costs, improve workflow or enhance functionality?
- Will the changes negatively impact patient access?

## Transition Planning

*Certification and Registration*
All current site registrations, health care provider registrations, pharmacy certifications, etc. must be transferred to the new system. It would be inappropriate to waste scarce health care resources requiring re-registration or re-certification. In addition, failure to re-register or re-certify could result in interruption to treatment of a serious disease or condition with severe consequences for the patient, unnecessary costs and additional workload.

*Data Preservation*
All existing patient data must be preserved in the new system as the REMS represents a source of patient history. Since health professionals are forced to document patient information and treatment in the REMS, it often serves this purpose for those using it. When there is a change in the provider or team caring for an individual patient, this information can be quite valuable in the care of patients.

*Overlap and Phase-in*
A change in the REMS system must never take place instantaneously. AAPP strongly recommends that switchovers be phased (overlapped) over an extended period of time during which the current and proposed REMS both operate. Such a phase-in helps prevent a "bottleneck" or even a crisis during which REMS phone systems, websites or call centers become overloaded. This phase-in preserves patient access. During a phase-in, AAPP recommends that all patients new to the medication or restarting the medication automatically be directed to the new system. Patients established on the medication would be slowly switched over. A provision to allow health care systems or prescribers to switch all of their patients on a specific date should also be offered. The phase-in should be planned for at least 90-120 days with the ability to extend it based on issues discovered during the phase-in.

*Dynamic Performance Assessment*
During the overlap or phase-in proposed by AAPP, regular evaluation of the new system as described in the *Testing of the New REMS System* should occur. This will permit issues to be resolved before they impact multiple patients, health care organizations and providers. Issues that arise during the overlap may delay the termination of the previous system.

## Failure Mode and Effects Analysis (FMEA)

AAPP strongly supports FMEA and planning for system failures. Part of the planning should include provisions for an emergency suspension of the REMS or specific provisions of the REMS should that become necessary to preserve medication access. Planning should also include a public dissemination of the information plan related to emergency suspension. Posting a notice on the FDA website is inadequate. Communication should include all of the delivery conduits and stakeholders noted in the section above entitled *Solicitation of Stakeholder Input.* FMEA and planning should also be undertaken for all existing REMS as they could experience some sort of unanticipated failure due to a variety of factors. Finally, preservation of patient access to a medication about which health care providers and patients have already been educated should be the FDA's primary concern.

**Metrics for Evaluation**

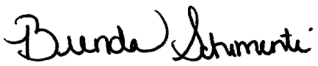
AAPP recommends that metrics include the survey elements noted in the *Testing of New REMS System* above. Both the current and proposed systems should capture:

- Contact volume (including phone, fax and email contacts)
- Type of contact (website issue, basic information issues, patient situation, etc.)
- Adverse events
- Interruptions in treatment
- Difficulty accessing medication due inability to locate a prescriber
- Difficulty accessing medication due to inability to locate a pharmacy
- Utilization data such as manufacturer/wholesaler data on drug sales/number of prescriptions/number of patients to detect change in access due to a change in the REMS.

AAPP strongly recommends that all future REMS agreements that the FDA enters into with manufacturers and that manufacturers enter into with their vendors, require that deidentified performance and clinical REMS data be made available to appropriate external reviewers. The availability of independent review data will reassure the public, patients and health care providers that each REMS is accomplishing its intended outcomes and assuring safety as intended without unanticipated negative consequences.

AAPP thanks the FDA for the opportunity to comment on the Proposed Changes to Third-Party Vendors for Risk Evaluation and Mitigation Strategies; Establishment of a Public Docket; Request for Comment. We look forward to continuing to work with the FDA to improve the REMS program and public health. Please contact Brenda Schimenti at bschimenti@aapp.org should you have any questions.

Sincerely,



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