FDA’s Risk Evaluation and Mitigation Strategies Program: What Pharmacists Need to Know

EDUCATIONAL OBJECTIVES

Upon completion of this activity, the participant should be able to:

1. Explain the evolution from risk minimization action plans (RiskMAPs) to REMS.
2. Identify key elements that may be included in REMS.
3. Describe the effect that a REMS has on the health care distribution system.
4. Summarize the existing challenges surrounding REMS.

Post-Test/Rationale

1. The pramlintide acetate REMS communication plan is designed to inform health care providers about:

   A. The importance of insulin dose reduction with pramlintide-insulin cotherapy
   B. The increased risk of severe hypoglycemia with pramlintide acetate
   C. The importance of appropriate patient selection when considering pramlintide acetate therapy
   D. All of the above***

Correct answer: D

The overarching goal of the pramlintide REMS program is to inform health care providers about the following: the increased risk of severe hypoglycemia associated with the use of pramlintide-insulin cotherapy, particularly in patients with type 1 diabetes mellitus; the importance of insulin dose reduction with cotherapy (remind clinical providers to counsel and instruct patients on insulin dose reduction to minimize the risk of hypoglycemia); and proper patient selection (pramlintide acetate is contraindicated in patients with hypoglycemia unawareness, confirmed gastroparesis, and hypersensitivity to any component of the product).

2. Which of the following statements is NOT correct regarding RiskMAPs and REMS?

   A. REMS programs may be imposed by the FDA before or after regulatory approval of a medicine
   B. The FDA may impose monetary penalties if REMS elements are violated
   C. Scheduled assessments of RiskMAPs and REMS are mandated by the FDA***
   D. All of the above

Correct answer: C

Refer to Table 1.

3. Which of the following schedules complies with REMS timetable for assessments?
A. 4 months, 3 years, 8 years after approval  
B. 18 months, 3 years, 7 years after approval***  
C. 1 year, 3 years, 5 years after approval  
D. 12 months, 3 years, 5 years after approval

Correct answer: B  
Additionally, to ensure that REMS programs are successfully decreasing the known risk of a drug, the FDA requires drug manufacturers to perform assessments of each program by dates that are 18 months, 3 years, and 7 years after the REMS is approved (timetable for submission of assessments), with additional dates when more frequent evaluations are necessary to ensure that the benefits of a medication outweigh its risks.

4. The Office of the Inspector General at the Department of Health and Human Services published a report highlighting which of the following?  
   
   A. The failure by the FDA to appropriately evaluate ETASUs***  
   B. The ineffectiveness of REMS communication plans  
   C. The removal of MedGuides from REMS when deemed unnecessary  
   D. The literacy level of content included in MedGuides

Correct answer: A  
A report published by the Office of the Inspector General at the Department of Health and Human Services revealed that the FDA completed only 1 evaluation of 32 possible ETASUs during the first 3 years after the enactment of FDAAA. As a result, the FDA has limited data to show that the other 31 REMS programs with ETASUs effectively ensure safe use or meet statutory requirements to minimize burdens on patients and the health care system.

5. Communication plans are directed toward:  
   
   A. The FDA  
   B. Patients  
   C. Health care providers***  
   D. Managed care organizations

Correct answer: C  
The FDA may determine that important information related to a drug should be disseminated directly to health care providers by a communication plan. These plans are intended for health care providers, not patients.

6. Which of the following elements may be part of elements to assure safe use (ETASU)?  
   
   A. Provider certification  
   B. Patient registration  
   C. Pharmacy certification  
   D. All of the above***
Correct answer: D
As defined in FDAAA, ETASUs may include ≥ 1 of the following components: health care providers who prescribe the drug must have special training or experience or become specially certified; pharmacies, practitioners, or health care settings that dispense the drug must become specially certified; the drug is dispensed to patients only in specific health care settings such as hospitals; the drug is dispensed only to patients who have evidence or other documentation of safe-use conditions, such as laboratory test results; each patient using the drug is subject to specific monitoring; and each patient using the drug must be enrolled in a registry.

7. The ESA APPRISE Oncology Program mandates all of the following ETASUs EXCEPT:

   A. Provider certification
   B. Hospital certification
   C. Documentation of safe use conditions
   D. Communication plan***

Correct answer: D
There are 3 ETASUs incorporated into the ESA APPRISE Oncology Program: (1) health care provider certification, (2) hospital certification, and (3) documentation of safe-use conditions.

8. With regard to the existing challenges surrounding REMS, pharmacy professional societies have expressed the need for all of the following EXCEPT:

   A. Reimbursement policies for the administrative burdens placed on pharmacies
   B. Releasing REMS that are no longer deemed necessary
   C. Standardization of REMS programs
   D. Application of Flesch-Kincaid grade level analyses to REMS education materials***

Correct answer: D
Pharmacy societies have encouraged the FDA to refine the existing REMS process by regularly reexamining each drug safety program and releasing additional REMS that are not considered necessary. Biosimilars and other proteins that are in various phases of clinical development probably will require additional pharmacovigilance by physicians, pharmacists, and nurses due to an overall lack of experience with these agents, and this emphasizes the importance of standardizing and/or eliminating undue administrative burdens on the health care system. The AMCP has urged the FDA to consider a compensation mechanism for pharmacists and pharmacies that handle REMS because the execution of REMS often results in administrative responsibilities that go beyond the usual dispensing process and patient care services provided by pharmacists.

9. Which of the following medications does not have a shared systems REMS?

   A. Epogen***
   B. Isotretinoin
   C. Mycophenolate
D. Extended-release opioids

**Correct answer:**
Refer to Table 4.

10. Potential drawbacks of limited distribution systems include:

A. Disruptions in continuity of care
B. The need for single-product contracts, increasing the economic and administrative burdens on managed care organizations
C. The need for additional patient and provider education to prevent medication access issues
D. All of the above***

**Correct answer: D**
Drug manufacturers often prefer to distribute specialty pharmaceuticals through certified pharmacies that market themselves as experts in handling specialty drugs in a way that reduces risks to patients. In such cases, this requirement becomes part of an ETASU protocol and can markedly affect patient access to select medications and increase the economic burden on the managed care organization. When a manufacturer distributes medication through a few mail order, specialty, or outpatient pharmacies, these pharmacies may not be in the managed care organization network. The managed care organization may be forced to enter into separate contracts with other pharmacies, and this may create the additional responsibility of managing single product contracts. These situations may necessitate additional patient and provider education to prevent access issues for patients who need specialty drugs or biologics, and this may raise operational questions for managed care organizations.