# Mitigating the Elements of REMS. Start with your P&T Committee. Committee meet REMS

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The speaker has no conflict to disclose.

## Audience Background

Please raise your hand if your response is yes to the following questions:

- P&T Member?
- P&T Leadership Role? (set agenda, frame issues)
- Your REMS based Drug Use Policy Concerns are resolved and the Process is Operating in a Flawless Manner?
- You would like REMS to go away?

**PERSONALLY**

I want to fully support these goals:

**I regard the goals of the REMS regulations:**

- Improve the safety of selected newly approved medications.
- Enhance the capability to react to safety concerns raised by recent studies.
- Help patients play a more active role in medical decisions.
- Collect observational data about the safety of selected medications.

**Changes to Committee Practices**

REMS/ ETASU included in:

- Formulary Request
- Formulary Monograph
- Formulary Recommendation
- On-Line Formulary
- Pharmacists to sponsor Formulary Action for newly invoked REMS/ETASU/RDDS.

**Formulary Request Form**

Example: Tolvaptan

There are 4 steps to add a medication to the Formulary:

1. Disclosure of potential conflicts of interest with Otsuka the manufacturer of tolvaptan (Samsca ™).
2. Submit a protocol for the use of this medication in patients at NMH. Your protocol should summarize the evidence supporting your recommendation and also include the indications, patient selection, status (first line, alternative agent etc), and precautions that you recommend. A typical protocol is one or two paragraphs in length.

Risk Evaluation and Mitigation Strategy (REMS): A REMS is enacted because of increased risks associated with overly rapid correction of serum sodium leading to osmotic demyelination. Each patient is to receive an FDA approved Med Guide. Please describe your plan for compliance.

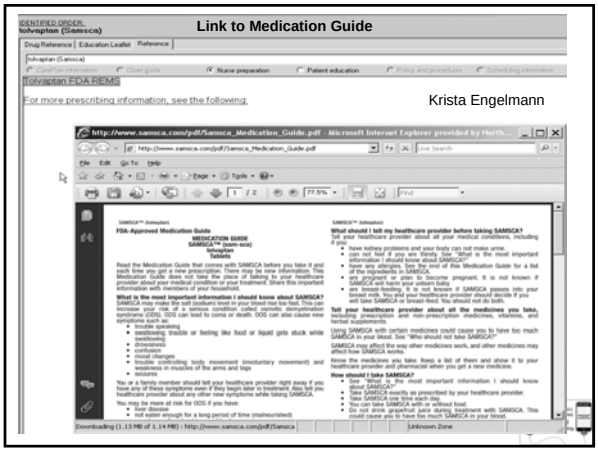
| Item | P&T Monograph | Finding / URL |
|---|---|---|
| Product dedicated website | http://www.samsca.com/ | |
| FDA News Item | FDA Approves Samsca to Treat Hyponatremia (May 22, 2009) http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm161945.htm | |
| REMS<br>A Risk Evaluation and Mitigation Strategy (REMS) is intended to manage a known or potential serious risk associated with a drug or biological product. A REMS will be required of the sponsor if the FDA believes it necessary to ensure that in use, the benefits of the drug or biological product outweigh its risks. A REMS can include a Medication Guide, Patient Package Insert, a communication plan, elements to assure safe use, and an implementation system, and must include a timetable for assessment of the REMS.<br>List of other drugs with REMS is at: http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm111350.htm<br><br>Bill Budris | The company was required to implement a REMS by the FDA. http://www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM187491.pdf<br>The REMS is required in order to decrease to lessen the potential risk of osmotic demyelination syndrome (ODS) by:<br>• Educating healthcare providers on the risk of overly rapid correction of serum sodium associated with tolvaptan and the need for initiating tolvaptan in a hospital to ensure proper titration and monitoring<br>• Informing patients of the serious risk associated with the use of tolvaptan, particularly the risk of osmotic demyelination syndrome<br>Elements of the REMS include:<br>• Medications Guide<br>• Communication Plan to Healthcare Professionals - involved in the prescribing, purchasing, dispensing or administration for both inpatient and outpatient settings at time of launch. (See details in following row) | |

## Committee Recommendation:

Tolvaptan is restricted to hepatologists, and intensivists. Use is restricted to FDA approved indications.

Orders for fluid restriction must be discontinued when tolvaptan is initiated.

Medication Guide must be selected when Tolvaptan is ordered.




## Raise your Hand if:

1. You think that Vendors are aware of REMS requirements?
2. You think that Formulary Sponsors are aware of REMS requirements?
3. You think that if the Formulary Sponsor received Speaker Training they are aware of REMS?
4. If you think that one company is more proactive about REMS than others?

## RECENT EXPERIENCES

| Medication | REMS | Formulary Sponsor | Action |
|---|---|---|---|
| Tolvaptan (Otsuka ) | Medication Guide | Unaware of REMS | Added to restricted formulary |
| Alvimopan (Adolor) | E.A.S.E. Program (ETASU) | Unaware of REMS* | Rejected |
| Romiplostim (Amgen) | NEXUS (ETASU) | Aware but voluntary | Proposal withdrawn |
| Deferasirox (Novartis) | RDDS rather than REMS EPASS Care System | Unaware | Proposal for off-label use tabled |
| Epoetin Alpha (Amgen) | APPRISE (ETASU) | Aware but assumed inpatients were exempt | Restrict use from oncology patients |

* Vendor induced Formulary Request

## Recent Experiences

| Medication | REMS | Formulary Sponsor | Action |
|---|---|---|---|
| Pradaxa (dabigatran) | Medication Guide | Unaware of REMS* | Added to restricted Formulary |
| Victoza (Liraglutide ) | Medication Guide | Unaware of REMS** | Added to restricted Formulary *** |
| | | | |
| | | | |
| | | | |

•Formulary Sponsor hoping to serve as a paid speaker
** Formulary Sponsor is a paid speaker
*** Pharmacists to provide Medication Guide

## Medication Guides

The best way to help patients understand the risks and benefits of treatment is to:

A. Staple the medication guide to a bag containing the filled prescription.
B. Have a clerical person inform the customer to ask their doctor if they have any questions.
C. You know the correct answer.

## Medication Guides

True of False

A. Medication Guides are the same as patient counseling sheets.
B. Patients will be re-assured about taking their medication after reading the Guide.
C. Medication Guides are lengthy and can run to 20 pages or more.
D. This is a potentially explosive situation.

## Statement for Medication Guides

Pharmacists - Please use the following template to guide your discussion about Victoza with NMH patients.

As you know all medicines have side effects. When a medication is brand new we don't always know what side effects to expect. Keep in mind that one day you may have serious side effects if you do not treat your diabetes. I have a pamphlet for you to read. This pamphlet was written by the company that sells this medication. It lists some of the conditions which might increase a person's chances of having a side effect. Most people do not have one of these conditions, and even if you do there is nothing to be alarmed about. Please look these over and tell your doctor if you or any family member has ever had one of the conditions that are listed. If you do your doctor will explain why this medication is necessary for you. Your doctor is expecting to have this conversation with you so please do not hesitate to discuss your concerns with her (him). If you are not sure how or what to discuss with your doctor please let me know so I can help you.

**CFR Title 21**
**April 1, 2010**

It applies primarily to human prescription drug products used on an outpatient basis without direct supervision by a health professional.

# REMS SURVEY

Survey Designed and Conducted by Bill Budris Drug Information Pharmacist

Northwestern Memorial Hospital

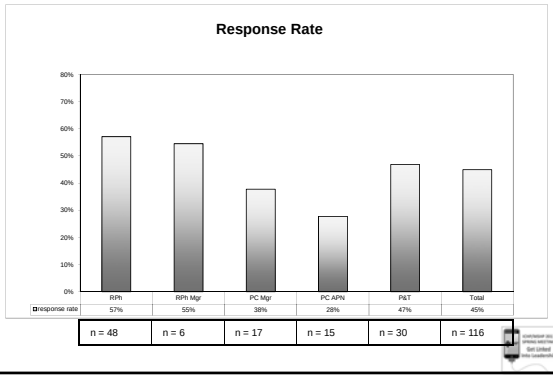
## REMS SURVEY

Web-based NMH survey, September 13-21, 2010

Survey Targets (n= 258)

- Staff pharmacists (84)
- Pharmacy Managers (11)
- Nursing Managers (45)
- Advanced Practice Nurses (54)
- P&T members other than RPhs (64)

## NMH Survey Results



## Survey Results (n = 116 )

**73.3% identified REMS correctly but otherwise REMS and implications poorly understood**

- *Asked if adequately informed about REMS* 6% said yes
- *Asked if REMS known to improve patient safety* 65.2% unsure
- *Asked to identify ETASU* 36% were correct
- *Asked if ETASU reduced serious medication errors* 66% unsure

## Survey Results

- *Asked if role clear with respect to REMS drugs used in practice area*:
  - Role not clear 89.7%
- *Asked which professionals are responsible for compliance with REMS*:
  - All are responsible 46.6%
  - Not Sure 41.4%

## Survey Results

- *Asked if off-label use of ETASU drugs will be possible*: 75.9% unsure
- *Asked if concerned time will be taken from other patient care*: 62.1% unsure
- *Asked where they first learned of REMS:* 54.9% this survey
- *Asked who requires REMS:* 44% correct - FDA
- *Asked if had direct REMS contact:* 16.8% had

## Actions

What did we do about it?

- REMS/ ETASU 101 presented to Medical Staff Leadership
- REMS/ETASU 101 presented to P&T Committee Leaders and Members
- REMS/ETASU 101 presented to NMH Pharmacy Staff
- REMS/ETASU 101 presented at Nursing Grand Rounds

**REMS/ ETASU P&T 101**

Raise your hand if you believe that Physicians prefer 10 page handouts over a single page.

Risk Evaluation and Mitigation Strategy (REMS)

Result of a negotiation between FDA and BigPharma and is based on occurrence of adverse events in clinical trials or seen post marketing. Goal for FDA is to ensure drug benefits outweigh risks, for BigPharma to ensure approval, broader indication, etc.

Why- failure of dear doctor/ dear pharmacist letters or boxed warnings, or black box warnings to influence risky prescribing. (FDA has a quaint belief in EBM)

REMS programs have 3 components

Level 1: Medication Guides and Patient Education

Level 2: Active communication of risk to prescribers- letters, professional meetings

Level 3: ETASUs (elements to assure safe use)

- Health care providers who prescribe the drug have particular training or experience or are specially certified.
- Pharmacies, practitioners, or health care settings that dispense the drug are specially certified.
- The drug is dispensed to patients only in certain health care settings, such as hospitals.
- The drug is dispensed to patients with evidence or other documentation of safe use conditions, such as laboratory test results.
- Each patient using the drug is subject to certain monitoring.
- Each patient using the drug is enrolled in a registry.

Drug class REMS will be implemented for extended release and long acting opioids and for LABAs. Implementation of a drug class REMS is scheduled for this year for ESA

Restricted Distribution Systems:

To date, there are 11 drugs under a REMS that requires restricted drug distribution through certified pharmacies:

- thalidomide, lenalidomide, romiplostim, bosentan, ambrisentan, dofetilide, alvimopan, fentanyl buccal soluble form, eltrombopag, vigabatrin, and olanzapine extended release injection.

## Research in Progress Report Abstract:

**Title**: The Remedy to REMS: A Pharmacy Team Initiative for Increased Patient Safety through Mitigation Strategies

**Investigators**: Juhi Jain, PharmD, Michael A. Fotis, R.Ph, William Budris, R.Ph, Neal Grosshans, M.S., R.Ph.

**Background/Purpose**: REMS (Risk Evaluation and Mitigation Strategies) were created by FDA to serve as post-marketing surveillance to improve safety for patients on targeted medications. Our objective is to develop a formal process at Northwestern Memorial Hospital for identifying practical mitigation possibilities; this study will provide data on the need for monitoring, outcomes, and time commitment. The team will consist of pharmacists, residents, and students.

**Methods**: The FDA and ASHP REMS lists were consulted to review medications for inclusion in this study. Data from a 6 month retrospective review of use, purchasing, formulary status and mitigation possibilities were used to narrow the list of drugs resulting in 6 study medications.

A "Mitigation Manual" was created with monitoring parameters, and protocol for each medication. Students will assess patients using a daily generated report; appropriateness of laboratory monitoring and of use will be measured.

The process will be reexamined and data will be evaluated for future development for policies or processes on REMS medications mitigation at NMH.

Identified Medications: Bosentan (Tracleer) Exanatide (Byetta) Teriparatide (Forteo) Dronedarone ( Multaq) Tolvaptan (Samsca)

## It is Time to:

**Goals**

- Improve the safety of newly approved medications.
- Enhance the capability to react to safety concerns raised by recent studies.
- Help patients play a more active role in medical decisions.
- Collect observational data about the safety of medications.

**Thank You!**

**Actions**

- Conduct post- Formulary approval use studies of clinical outcomes
- Focus studies on safety concerns
- Go beyond stapling a computer generated handout to a paper bag
- Continue to focus Committee sponsored use studies on safety concerns

**Its about Time!**

ICHP/MSHP 2011 Spring Meeting
Changes in Pharmacy Practice Session: Mitigating the Elements of REMS
Michael A. Fotis, BS Pharm
121-000-11-010-L04-P
121-000-11-010-L04-T

Post Test Questions:

1. Choose the most correct answer
   A. Vendors are all aware of REMS requirements
   B. Formulary Sponsors are all aware of REMS requirements?
   C. Formulary Sponsors completing Speaker Training are aware of REMS?
   D. There is a bit of confusion in the industry about REMS.

2. The best way to help patients understand the risks and benefits of treatment is to:
   A. Staple the medication guide to a bag containing the filled prescription.
   B. Have a clerical person inform the customer to ask their doctor if they have any questions.
   C. Have a conversation with the patient.

3. Please answer True or False
   A. Medication Guides are the same as patient counseling sheets.
   B. Patients will be re-assured about taking their medication after reading the Guide.
   C. Medication Guides are lengthy and can run to 20 pages or more.