



#### I regard the goals of the **PERSONALLY REMS regulations:** Improve the safety of selected I want to newly approved medications. fully support Enhance the capability to these goals: 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:

- Disclosure of potential conflicts of interest with Otsuka the manufacturer of tolvaptan (Samsca ™).
- 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.

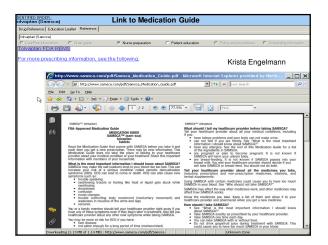


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#### **Committee Recommendation:**

- 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.





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Romiplostim (Amgen)	NEXUS (ETASU)	Aware but voluntary	Proposal withdrawn	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	Possibly to Restrict use from oncology patients	
* Vendor induced Formulary Request				

Recent Experiences				
Medication	REMS	Formulary Sponsor	Action	
Pradaxa (dabigatran)	Medication Guide	Unaware of REMS*	Sponsor disqualified	
			What did we decide?	
* Formulary Sp	oonsor hoping to serve a	s a paid speaker		

#### **REMS SURVEY**

Survey Designed and Conducted by Bill Budris Drug Information Pharmacist Northwestern Memorial Hospital

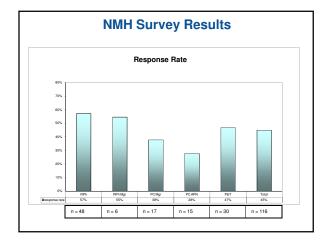


Web-based NMH survey, Pharmacy Managers (11) September 13-21, 2010

#### Survey Targets (n= 258)

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





#### 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 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**

about it?

- What did we do 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**



#### It is Time to:

- 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!





## **How REMS Impact Hospitalized Patients**

- · Restricts access to medications
- Delays access to medications
- Complicates access to medications



#### **Restricted Access to Medications**

- Vigabatrin (Sabril®)
  - FDA-approved for treatment of infantile spasms; refractory complex partial seizures not controlled by usual treatments
  - Boxed warning for vision loss
    - Vision should be assessed to the extent possible at baseline (no later than 4 weeks after initiation), at least every 3 months during therapy and at 3 to 6 months after discontinuation. Once detected, vision loss is not reversible.



#### **Restricted Access to Medications**

 Pediatric patient with infantile spasms is on vigabatrin at home and is emergently admitted to the Cleveland Clinic Children's Hospital



#### **Restricted Access to Medications**

- Per REMS program for vigabatrin (SHARE), Cleveland Clinic inpatient pharmacy <u>cannot</u> obtain medication because:
  - 1) Vigabatrin is only available from four select specialty pharmacies in the United States
  - 2) Specialty pharmacy will only send medication to patient's home once all aspects of REMS program for vigabatrin are met



#### **Restricted Access to Medications**

- Patient safety issue if family does not bring in medication from home
- Difficulty in providing the best care to a pediatric patient if inpatient pharmacy cannot obtain the medication
- Stress and burden on family in an already stressful situation



#### **Restricted Access to Medications**

- Discuss with family reason for not being able to obtain vigabatrin
- Request family to bring in vigabatrin from home (travel time and distance)
- Order for patient to "take own medication from home" (policy and procedure)
- > Identify vigabatrin (pharmacist)
- > Inpatient pharmacies need access to medications



#### **Delayed Access to Medications**

- Dofetilide (Tikosyn®)
  - FDA-approved for maintenance of normal sinus rhythm in patients with chronic atrial fibrillation/atrial flutter of longer than 1-week duration who have been converted to normal sinus rhythm; conversion of atrial fibrillation and atrial flutter to normal sinus rhythm
  - · Boxed warning for arrhythmias
    - Must be initiated (or reinitiated) in a setting with continuous monitoring and staff familiar with the recognition and treatment of life-threatening arrhythmias. Patients must be monitored with continuous ECG for a minimum of 3 days, or for a minimum of 12 hours after electrical or pharmacological cardioversion to normal sinus rhythm, whichever is greater.



#### **Delayed Access to Medications**

- Adult patient with chronic atrial fibrillation is on dofetilide at home and is admitted to the Cleveland Clinic Heart and Vascular Institute.
- Per REMS program for dofetilide, prior to dispensing, it must be verified that the physician/prescriber is a "certified" Tikosyn® prescriber.



#### **Delayed Access to Medications**

- Delay in patient care because updated list of prescribers may not be readily available to the pharmacist
- Delay in patient care if patient is admitted during night shift because there may not be a "certified" Tikosyn® prescriber on site
- Challenge to provide best care to patient due to potential lag time in patient receiving the needed medication



#### **Delayed Access to Medications**

- Pharmacy system (or CPOE system) contains list of "certified" Tikosyn® prescribers and is updated regularly
- Third shift ("off shifts") notifies first shift to inform a "certified" Tikosyn® prescriber to evaluate patient
- > Patient misses one dose of dofetilide
- Standard database for certified prescribers for REMS requiring certification/registration



#### **Complicated Access to Medications**

- Erythropoiesis-Stimulating Agents (ESAs)
  - \* FDA-approved for treatment of anemia (elevate or maintain red blood cell level and decrease the need for transfusions) associated with chronic renal failure (including patients on dialysis and not on dialysis); treatment of anemia due to concurrent chemotherapy in patients with metastatic cancer (nonmyeloid malignancies)
  - Boxed warning
    - Increased mortality, serious cardiovascular events, thromboembolic events, stroke and increased risk of tumor progression



#### **Complicated Access to Medications**

 Adult patient is admitted to Cleveland Clinic and needs to have an ESA initiated while hospitalized



#### **Complicated Access to Medications**

- Per REMS program for ESAs (APPRISE),
  - ESA is dispensed to patients with evidence or other documentation of safe use conditions
  - Health care professionals (i.e., prescribers) and "hospital designees" must be specially certified
     Online certification and enrollment, including APPRISE number

    - Delay in patient care because updated list may available to the pharmacist
    - Delay in patient care if patient is admitted when there may not be a "certified" prescriber in the hospital



#### **Complicated Access to Medications**

- Per REMS program for ESAs (APPRISE),
  - Certified health care professional and patient documentation of risk:benefit discussion
    - Paper (ESA APPRISE Oncology Program Care Professional Acknowledgement Form)

    - Signature of prescriber and patient
       Patient refuses to sign acknowledgement form
  - ❖ Maintenance of Acknowledgement Form (random
    - Pharmacist's time to ensure compliance with APPRISE requirements, as well as to manage and maintain required paperwork



#### **Complicated Access to Medications**

- Pharmacy system (or CPOE system) contains list of "certified" APPRISE prescribers and is updated regularly
- Third shift ("off shifts") notifies first shift to inform a "certified" APPRISE prescriber to evaluate patient
- Inpatient initiation requires discussion between patient and "certified" APPRISE prescriber (signatures on form)
- Hospital designee must maintain required forms (hard copy versus scanned form)



#### **Complicated Access to Medications**

- Standard database for certified prescribers for REMS requiring certification/registration
- > Standard process to maintain and track forms for compliance and potential audits

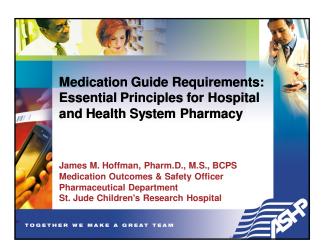


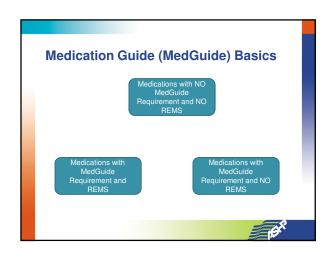
#### **Conclusions**

- The intent of REMS is for the appropriate and safe use of medications in patients.
- However, select REMS can restrict, delay, or complicate access to medications in hospitalized patients.
- This can lead to problems with patient care, patient safety, and overall patient satisfaction.
- Hospital pharmacists need to be able to effectively manage REMS, including educating both health care professionals and patients regarding medication access.

#### **Conclusions**

- In the future, there will be more REMS that affect access to medications in hospitals.
- Therefore, if an effective system for a REMS program in a hospital is initiated, implemented, and validated, it should be used for other similar REMS programs (i.e., standardization).





# **Key Medication Guide Points for Hospital/Health-System Pharmacy**

- Patients being cared for in a hospital and are administered a drug that requires a MedGuide need to be provided a MedGuide if:
  - The patient is given/dispensed the drug to take home
  - The patient is dispensed the drug from hospital based outpatient pharmacy for self-care/self-administration
  - The REMS documentation requires a MedGuide to be provided at specified points in the patient care process.



#### **Key Points to Note**

- Federal Law related to Medication Guide (MedGuide) requirements for NON-REMS drugs is 21 CFR 208
  - MedGuide needs to be provided when drug is dispensed to a patient
  - Dispensed is defined as a prescription that is provided to a patient for self administration.
- If the drug has a REMS, other requirements for the REMS must be fulfilled



#### **Key Elements of REMS**

- REMS in general have three main components called "REMS Elements"
  - \* Part A: Medication Guide
  - Part B: Communication Plan
  - \* Part C: Elements to Assure Safe Use
    - Can include prescriber education
    - Can include pharmacist education
    - Can include pharmacist/pharmacy/prescriber registration
    - Can include mandatory lab tests
    - Can include patient agreements/consents
    - Can include use of Medication guide in ETASU noted above



#### **Medication Guide Scenarios**

- Scenario 1: Drug approved by FDA with NO MedGuide
- Scenario 2: Drug Approved by FDA with MedGuide per 21 CFR 208
- Scenario 3: Drug Approved by FDA with REMS (includes certain past RiskMap drugs):

  - Case 1: "Part A" MedGuide requirement per 21 CFR 208
    Case 2: "Part A" MedGuide requirement per 21 CFR 208 PLUS
    in additional points in patient care process (i.e. before each infusion of drug)
  - Case 3: MedGuide requirement per "1" or "2" PLUS dictated by an element to assure safe use (ex. Required as a step in the patient/provider consent document at point of prescribing)



#### **REMS Drugs Cases**

- ACTOPLUS MET (ploglitazone hydrochloride and metformin hydrochloride) tablets

  A Medication Guide will be dispensed with each ACTOPLUS MET prescripton. The Medication Guide will prescriben. The Medication Guide will prescriben. The Medication Guide will prescribing information as a perforated attachment. Each packaging configuration including bottles, sample cards, and trays will contain a Medication Guide as part of the packaging and included as part of the packaging and ACTOPLUS MET. Takede has met the requirements of 21 CFR 208.24 for distribution and dispensing of the Medication Guide.

# Case 1: "Part A" - MedGuide requirement per CFR 208 • ACTOPLUS MET (pigglitazone 2005 in additional points in patient care process

- ACTEMRA® (tocilizumab)
- Human interleukin-6 receptor inhibitor

   A. Medication Guide (FDCA Section 505-1 (e)(2))
- (e)(2) In accordance with 21 CFR 208.24, a Medication Guide will be included in each ACTEMRA® vial package. This Medication Guide should be dispensed to each
- prior to each ACTEMRA® administration

  The Medication Guide will also be
  available via sales representatives, the
  ACTEMRA® patient and professional
  websites, and a toll-free product
  information line (1-800-ACTEMRA).

  Please see the appended Medication
  Guide (Attachment A).



#### REMS Drugs Case – Epoetin Alfa

- BL 103234 EPOGEN®/ PROCRIT® (EPOETIN ALFA)
- Medication Guides will be provided in accordance with 21 CFR Part 208
- Retail or Hospital Outpatient Pharmacy Services

  With every dispensing pack of Epogen Procrit in a printable
  format that can be downloaded from the epogen.com or
  procrit.com websites or by contacting the Medical
  Information Department toll-free numbers for each
  product.
- Physician Offices/Clinics/Hospital Inpatient and In-Clinic Services/Dialysis Centers/
- the product is continued.

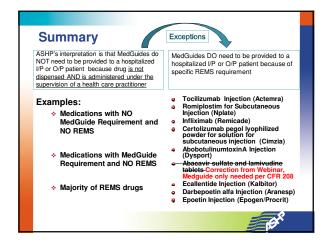
  en will ensure that a sufficient quantity of Medication continues.

  en will ensure that a sufficient quantity of Medication Guides are made available to physician offices, clinics, hospital inpatient pharmacies, and in-clinic services dispais centers that administer Epogen/Procrit to provide to the patient or the patient's representative when the product is dispensed.
- when the product is dispensed. incation Guides will also be made available to these settings through field-based personnel upon request, in a printable format that can be downloaded from the epogen.com or procrit.com websites, or by contacting the Medical information Department toll-free numbers for
- gen will ensure that HCPs, clinics, and hospitals are notified and provided with updated Epogen/Procrit Medication Guides if they are materially revised.

- Case 3 : MedGuide requirement per "1" or "2" PLUS
  dictated by an element to assure safe use
  or 2" PLUS dictated by
  an element to assure safe use
  an element to assure safe use (continued)

  - (excerpt of one of the more than 40 steps of the elements to assure safe use)
  - Il provide an Epogen/Procrit Medication Guide in accordance with 21 CFR Part 208 to each oncology patient. In addition, I will provide an Epogen/Procrit Medication Guide to



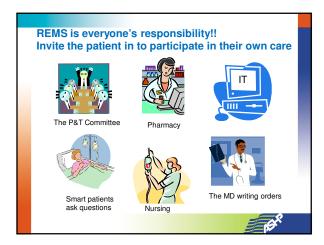


#### What next?

- ASHP and its members will need to communicate when REMS MedGuide anomalies exist
- ASHP and its members need to continue to advocate with FDA for standardization of REMS processes so implementation can be more efficient and effective for patients and providers
- More resources available at http://www.ashp.org/REMS







### **REMS** are important because they

- Provide an opportunity to rebalance risks and benefits
- Enable access to medications that otherwise would be unavailable due to a high risk to benefit ratio
- Provide a method of communicating important information about risks to all stakeholders
- Are a valuable new tool for Patient Safety



#### **Health System Strategies**

- Education about REMS
  - P&T, Medication Safety Committee, Risk Management
     Pharmacy, Nursing, Medical Staffs
- Identify central pharmacy resource to coordinate REMS programs
- Make use of IT!!
  - Use of order sets to ensure criteria met
- Model after investigational drug services?
- Include as part of Formulary Process
- Your contribution to a steady movement towards patient and family centered care





#### **Building a culture of patient safety**

- A healthy patient safety culture is fundamental to safe medication-use processes.
- An effective patient safety culture is characterized by a learning environment where patient safety events are carefully analyzed.
- Process and system failures are then proactively improved in a non-biased and non-threatening manner, and employee's behavioral choices are also carefully managed.
- Learn how you can assess, develop, and improve the culture of safety in your department and institution



#### **Conclusion**

- Press for standardization of REMS
- Assess and reduce burden on health care system
- Balance with risk and benefit for patient access
- Push forward to maximize the use of a relatively easy low tech way of impacting patient safety
- First and foremost.....never lose sight of the patient and the family



