



Comprehensive Pharmacovigilance in the VA: A Focus on Medication Safety Surveillance and Risk Reduction Through Intervention

**VA Center for Medication Safety
(VAMedSAFE)**

HFN Meeting





Comprehensive Overview of Medication Safety in VA

**Fran Cunningham, Pharm.D.
Associate Chief Consultant, PBM
Director, VA Center for Medication Safety**





GOAL of VAMedSAFE Program

- Track and evaluate high risk agents, high volume agents, and NMEs with potential risks in the Veteran population
- Determine rates and risks of ADEs associated with specific agents
- Maintain VA's national drug safety program with emphasis on:
 - Utilizing integrated databases as the foundation of the VA comprehensive pharmacovigilance program
 - Enhancing spontaneous ADE reporting for system based changes and enhancement of drug safety efforts
 - Collaboration on medication safety efforts with other Federal Agencies





VAMedSAFE Programs

- **Drug Surveillance**
 - Rapid Cycle Database Evaluations (Active)
 - VA ADERS (Passive)
- **National Medication Use Evaluations (MUE)**
- **Risk Reduction/Medication Use Evaluation Tracker (MUET) - Intervention**
- **Medication Safety Communication**
- **Interagency Medication Safety Collaboration**
- **Research**





EXAMPLES





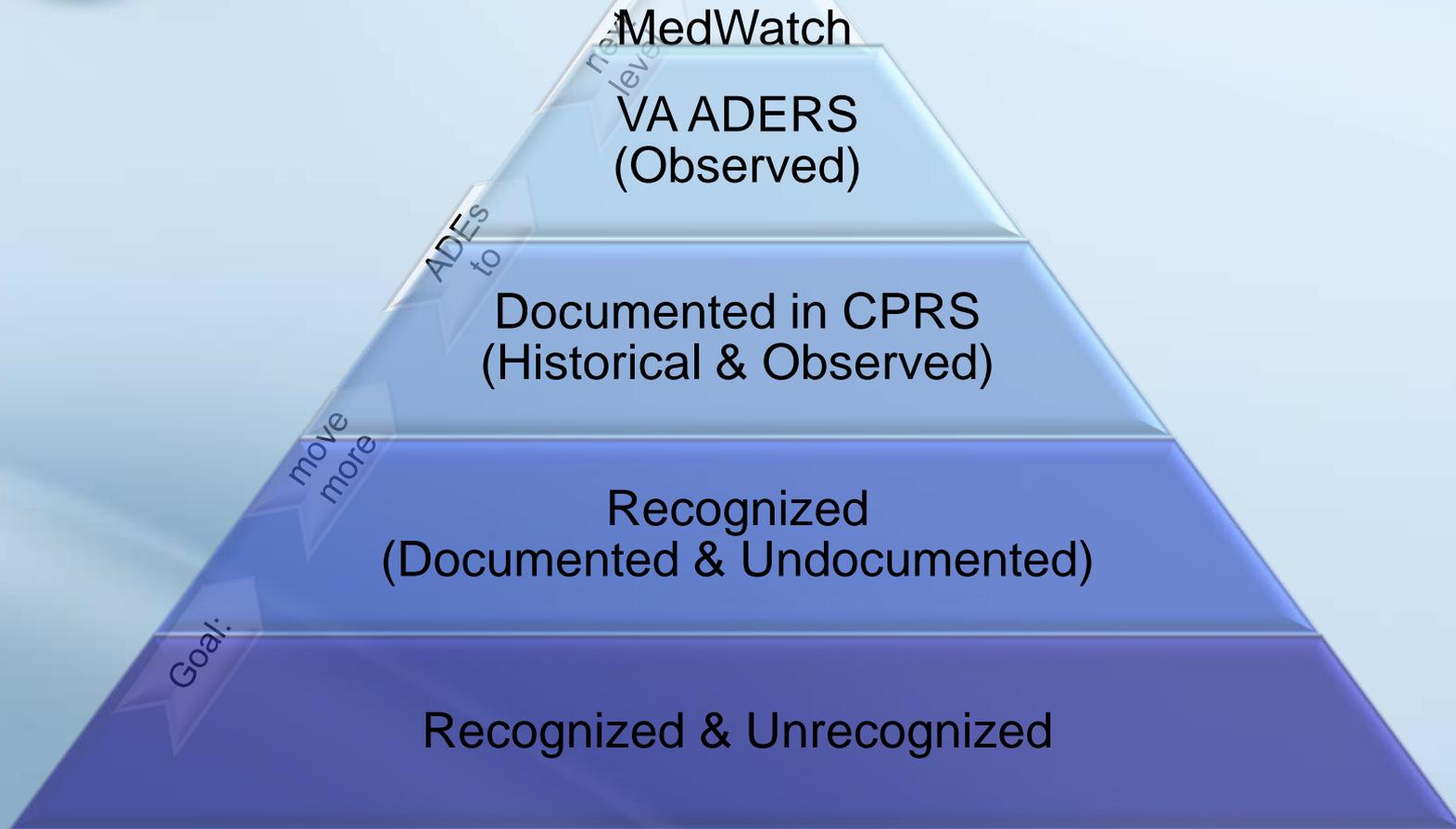
EXAMPLES OF DATABASE SURVEILLANCE/ RAPID CYCLE EVALUATIONS

- Antipsychotics
- High Dose Statins
- PPIs
- Opioids
- Prasugrel
- Natalizumab
- Varenicline
- Vaccines
- Ticagrelor
- TSOACs
- Dimethylfumarate
- Hep C Agents



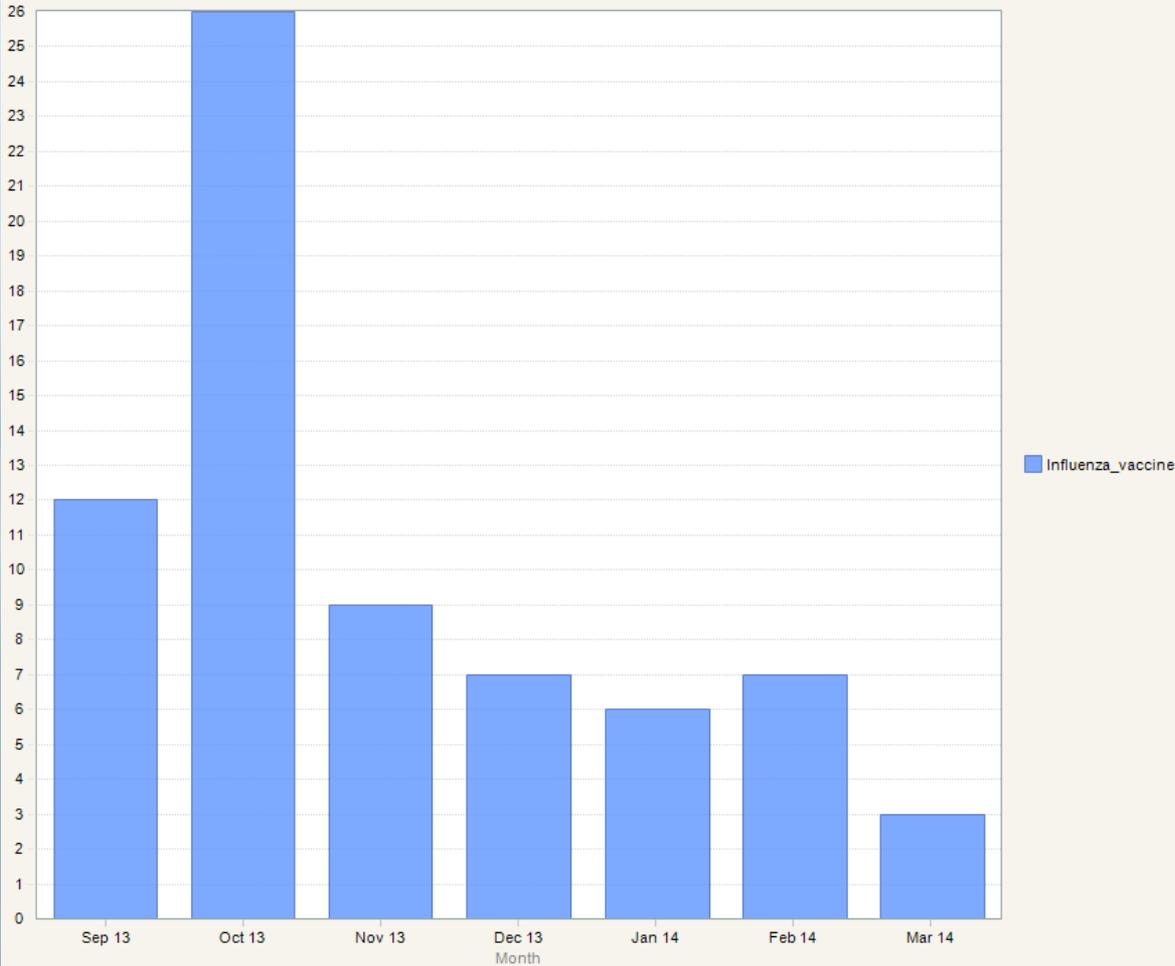


VA ADERS NATIONAL DATABASE





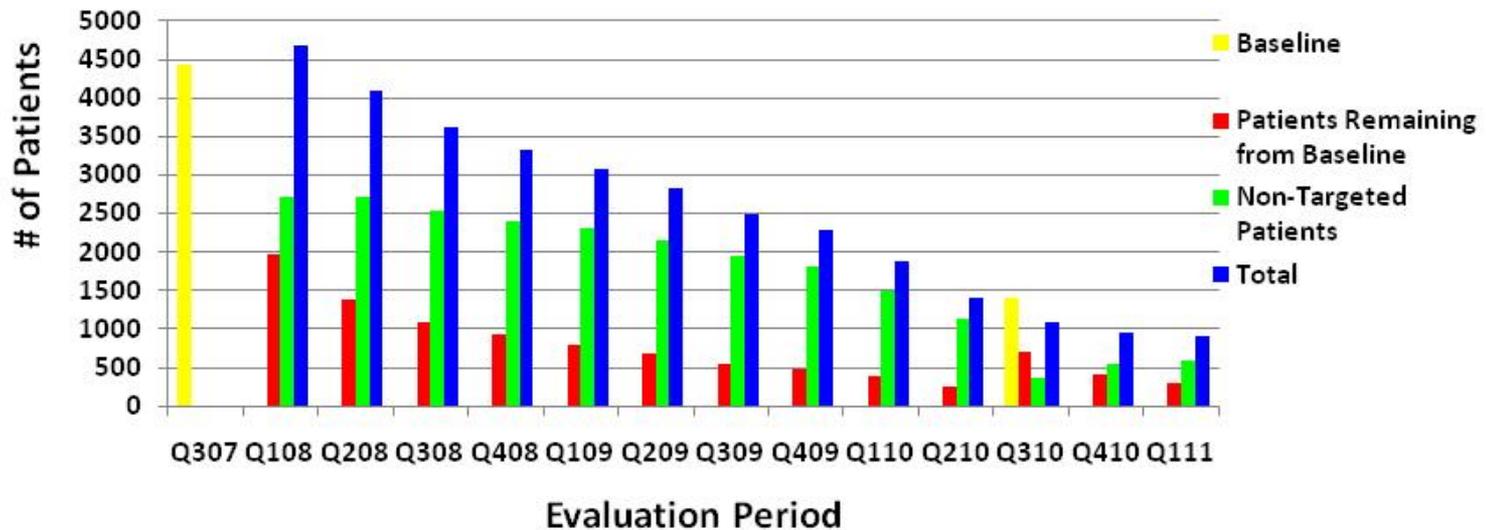
Influenza ADE Reports to VA ADERS by Month September 2013 to April 2014





Glyburide Risk Reduction/MUET

Patients with Active Prescriptions for Glyburide,
Age 65+ and SCr \geq 2 mg/dl





NATIONAL PBM DRUG SAFETY ALERTS

- **Types**
 - **Bulletins**
 - **Newsletters**
- <http://www.pbm.va.gov/VACenterForMedicationSafety-BulletinsAndNewsAlerts.aspx>



NATIONAL PBM BULLETIN

March 26, 2013

DEPARTMENT OF VETERANS AFFAIRS VETERANS HEALTH ADMINISTRATION (VHA)
PHARMACY BENEFITS MANAGEMENT SERVICES (PBM), MEDICAL ADVISORY PANEL (MAP),
AND CENTER FOR MEDICATION SAFETY (VA MEDSAFE)

SODIUM BIPHOSPHATE/SODIUM PHOSPHATE ENEMA PRODUCT USE AND FATAL OUTCOME

I. ISSUE

A recent adverse event report described a fatal outcome related to the use of Sodium Biphosphate/Sodium Phosphate enemas used to treat constipation.

II. BACKGROUND

A patient received multiple Sodium Biphosphate/Sodium Phosphate enemas in less than 12 hours. The patient subsequently developed hypernatremia, hypocalcemia, hypovolemia, acute kidney injury, and later died.

III. DISCUSSION

Saline laxative products containing Sodium Biphosphate/Sodium Phosphate are commercially available under the brand name Fleet® Enemas. When used in appropriate dosages and for a limited time, most laxatives do not pose a risk for serious adverse events such as diarrhea, GI irritation, and fluid/electrolyte depletion. However, prolonged use or overuse can lead to dehydration as well as fluid and electrolyte imbalances, possibly resulting in hyponatremia, hypotension and volume depletion, hyperphosphatemia, hypo- or hyperkalemia, metabolic acidosis, severe hypocalcemia, renal failure, EKG changes (i.e., prolonged QT interval), generalized tonic-clonic seizures, and loss of consciousness. Selected adverse effects from Sodium Biphosphate/Sodium Phosphate products include:

- **Mild:** bloating, stomach pain, tightness in the throat, dizziness, headache;
- **Severe:** rectal bleeding, lack of bowel movements after use, sores or ulcers around rectum, seizures, blackouts, convulsions, irregular heart rate, decreased urination, increased thirst, nausea, vomiting, confusion, swelling, weight gain, shortness of breath, electrolyte abnormalities.

IV. PROVIDER RECOMMENDATIONS

The affected facility engaged in the following actions to safeguard against future medication error with Sodium Biphosphate/Sodium Phosphate enema products.

1. Remove "FLEETS" or "FLEET'S" or "FLEET'S" as a synonym to order Sodium Biphosphate/Sodium Phosphate enema as it is a general term for enemas and does not provide further product detail. This would require the order entry selection of the Sodium Biphosphate/Sodium Phosphate enema by name and strength, prompting the provider to focus on the differences among the products (i.e., mineral oil, bisacodyl, phosphate, etc.) and choose the appropriate agent based on the patient's clinical presentation.
2. Add a comment in the drug file to highlight "NO MORE THAN 1 PHOSPHATE ENEMA IN 24 HOURS" for Sodium Biphosphate/Sodium Phosphate enema products. See Figure 1 on Page 2.
3. Ensure education for providers and applicable health care staff regarding the appropriate use of enemas as well as the risks of their chronic use, overuse, or misuse, specifically:
 - Using more than one enema in 24 hours can be harmful.
 - Exercise caution in patients with renal impairment, cardiac disease, colostomy, or pre-existing electrolyte

disturbances as well as those on concomitant therapy that may affect serum electrolyte concentrations since dehydration, hypocalcemia, hyperphosphatemia, hypernatremia, hypokalemia, and acidosis may occur.

V. REFERENCES

1. Internal Data.
2. McEvoy GK, ed in chief, Snow ED, ed. *AHFS: Drug Information*. Bethesda, MD: American Society of Health-System Pharmacists; 2012: 2950-2954.

Figure 1. One facility added the following verbiage to the ordering template for Sodium Biphosphate/Sodium Phosphate enema products: "NO MORE THAN 1 PHOSPHATE ENEMA IN 24 HOURS". This may serve as one option for how to inform providers at the site level of this safety risk.

The screenshot shows the 'Outpatient Medications' window. At the top, the drug name is 'PHOSPHATES ENEMA <SODIUM BIPHOSPHATE/SODIUM PHOSPHATE ENEMA >'. Below this, a blue banner contains the text 'NO MORE THAN 1 PHOSPHATE ENEMA IN 24 HOURS'. The main table has columns for 'Dosage', 'Complex', 'Route', and 'Schedule'. The 'Route' column is set to 'RECTAL'. The 'Schedule' column is set to '6XD AC+HS BEDTIME BEDTIME PRN BID BID-PRN BID-BEFORE-MEALS DAILY'. There is a 'Comments' field at the bottom of the table area. At the bottom of the window, the drug name is repeated: 'SODIUM BIPHOSPHATE/SODIUM PHOSPHATE ENEMA INSERT INTO RECTUM' with 'Quantity: 0 Refills: 0'. Buttons for 'Accept Order' and 'Quit' are visible.

ACTIONS

- **Facility Director (or physician designee):** Forward this document to the Facility Chief of Staff (COS).
- **Facility CDS and Chief Nurse Executives:** Forward this document to all appropriate providers who prescribe these medications (e.g., primary care providers, nursing staff, and pharmacy staff, including contract providers, etc.). In addition, forward to the Associate Chief of Staff (ACOS) for Research and Development (R&D). Forward to other VA employees as deemed appropriate.
- **ACOS for R&D:** Forward this document to Principal Investigators (PIs) who have authority to practice at the facility and to your respective Institutional Review Board (IRB).



MEDICATION SAFETY IN SECONDS

A MONTHLY PUBLICATION FROM VA MEDSAFE:
VA'S COMPREHENSIVE PHARMACOVIGILANCE CENTER

Helping to achieve safe medication use

FORMULARY IMPLICATIONS OF KETOCONAZOLE SAFETY ISSUES

In July 2013, FDA limited usage of ketoconazole oral tablets due to:

- Potentially fatal liver injury;
- Risk of drug interactions that may lead to QT prolongation; and
- Adrenal gland problems.

Complete details regarding these safety issues can be found in the FDA's Drug Safety Communication (<http://www.fda.gov/Drugs/DrugSafety/ucm362415.htm>) as well as the last issue of *Medication Safety in Seconds* (Issue 7, Volume 3, July/August 2013). As such, ketoconazole oral tablets are now FDA-indicated only for the treatment of blastomycosis, coccidioidomycosis, histoplasmosis, chromomycosis, and paracoccidioidomycosis in patients with suboptimal response and/or intolerance to other treatments. The use of ketoconazole tablets in *Candida* and dermatophyte infections is no longer indicated. Ketoconazole should only be used when other effective antifungal therapy

is not available or tolerated and the potential benefits outweigh the potential risks.

Although not FDA-approved, ketoconazole is prescribed (off-label) as an alternative agent for prostate cancer and is rarely used off-label in Cushing's syndrome. Consequently, ketoconazole will now be listed on the VA National Formulary (VANF) with a restriction to hematology-oncology, as opposed to the former anti-infective restrictions. As a result, non-formulary review will need to occur for uses in infectious diseases, dermatology, endocrine, etc.

REFERENCES:

FDA Drug Safety Communication: FDA limits usage of Nizoral (ketoconazole) oral tablets due to potentially fatal liver injury and risk of drug interactions and adrenal gland problems. <http://www.fda.gov/Drugs/DrugSafety/ucm362415.htm>. Accessed 09/24/2013.

Contributed by:

Melinda Neuhauser, Pharm.D., M.P.H.

IN THIS ISSUE:

- ▶ FORMULARY IMPLICATIONS OF KETOCONAZOLE SAFETY ISSUES.....1
- ▶ MEDICATION SAFETY NEWS FROM THE VA NATIONAL PHARMACY BENEFITS MANAGEMENT SERVICES (PBM) AND THE FOOD AND DRUG ADMINISTRATION (FDA).....1,2
- ▶ VASOPRESSIN AND HYDRALAZINE POTENTIAL LOOK-ALIKE CONFUSION3



VA PHARMACY BENEFITS MANAGEMENT SERVICES (PBM)

PBM maintains VA's national drug formulary, as well as promotes, optimizes, and assists VA practitioners with the safe and appropriate use of all medications.

VA CENTER FOR MEDICATION SAFETY (VA MedSAFE)

VA MedSAFE performs pharmacovigilance activities; tracks adverse drug events (ADEs) using spontaneous and integrated databases; enhances education and communication of ADEs to the field; and promotes medication safety on a national level.

EDITOR-IN-CHIEF

Marie Sales, Pharm.D.

VA Pharmacy Benefits Management Services (PBM) & Center for Medication Safety (VA MedSAFE); 1st Avenue—1 Block North of Cermak Road | Building 37; Room 139 | Hines, Illinois | 60141; www.pbm.va.gov

NEWSWORTHY...

from the pbm

- Nova Max Glucose Test Strips Recall Due To Falsely Elevated Blood Glucose Results – 08/14/13 – [National PBM Communication](#)
- Valproate Use During Pregnancy and Lower IQ in Children Exposed – 08/06/13 – [National PBM Bulletin](#)

(continued on page 2)



Collaboration with Federal Agencies

- **FDA**
- **Department of Defense Pharmacovigilance Center**
- **HHS/CDC**
 - **Vaccine safety**





Risk Reduction Through Intervention: Medication Use Evaluation Tracker (MUET)

Muriel Burk, Pharm.D.





MUET Process

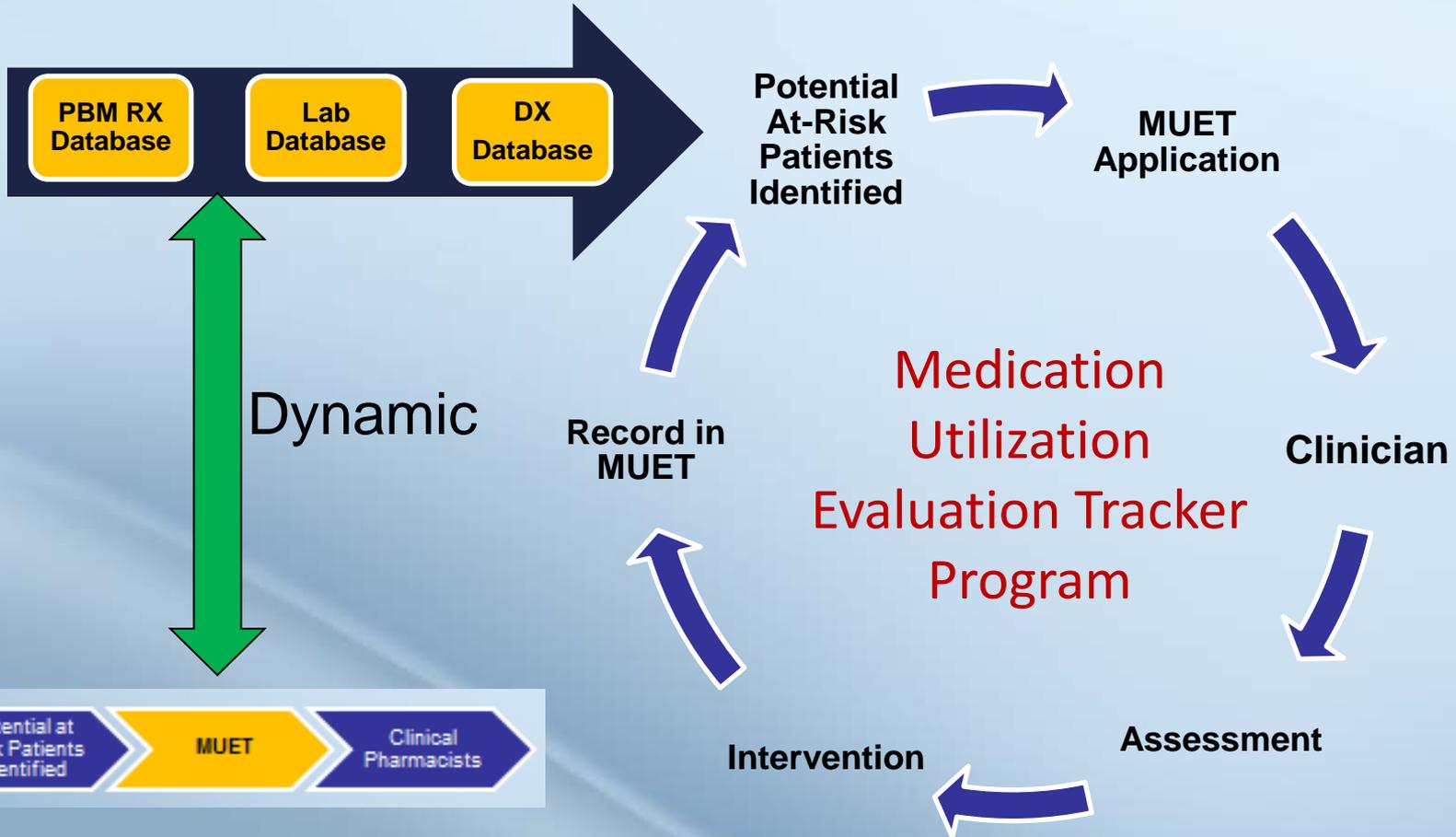
GOAL:

Address and Communicate High Risk Veteran Populations to VA Medical Centers





MUET Closes the Loop





5 Current MUET Initiatives

Initiative	Frequency	Risk Criteria Screened	Data Sources
ESA	Monthly	<ul style="list-style-type: none">Based on Hemoglobin and Ferritin Levels	RX, Lab
TSOAC	Monthly	<ul style="list-style-type: none">Based on Identification of Risk Factors, Bleeding Events, and Dosing	RX, Lab, DX
Prasugrel/ Ticagrelor	Quarterly	Active prasugrel or ticagrelor for greater than 12 consecutive months	RX
Women on Warfarin	Quarterly	Female of childbearing age on warfarin and who have no evidence of receiving contraception or surgical sterilization	RX, DX, CPT
MRA in HF	Quarterly	New/active spironolactone or eplerenone user with absence of serum potassium levels within 90 days following the first RX release	RX, DX, Lab



MRA in HF MUET Criteria

Objective: Identify potentially at-risk heart failure patients being prescribed an MRA without a documented VA potassium follow-up within the first 3 months of therapy initiation.

Criteria	Definition
Heart failure	At least one inpatient diagnosis of any rank or two outpatient diagnoses identified by ICD-9 code within 2 years prior to index RX date.
Mineralocorticoid Receptor Antagonist (MRA) Therapy	Eplerenone Spironolactone (Including combination products)
New and current MRA user	Absence of VA RX for MRA within 6 months prior to index RX date. Patient must have at least one day of therapy during month of data extraction.
Potassium Screening	Absence of VA serum potassium results within 90 days after initial MRA Rx date and up through time of data extraction



MRA in HF MUET Completed Interventions

Completed Interventions	All Time*
Criteria for Use Met – VA potassium available upon review	77
Continue Therapy - Lab/test Ordered	36
Continue Therapy – Not a new RX	24
Continue Therapy – Lab obtained outside VA	17
Drug Discontinued - Drug Discontinued Prior to Review	12
Continue Therapy - Criteria Not Met (Other reason - documented in chart)	11
Patient expired - not related to drug	9
Drug Discontinued - Other Reason	8
Drug Discontinued - No Longer Indicated	1
Continue Therapy – Criteria for safe use NOT met (Provider declined recommendation – reason documented in chart)	1

*MRA in HF MUET initiative has 2 completed cycles - FY14 Qtr 3 & Qtr 4



MUET Access



To access the MUET application, all you need is:

CPRS Log-in Credentials

https://vaww.cmop.med.va.gov/MedSafe_Portal/





Department of
Veterans
Affairs

MedSafe - CPASS
(Clinical Pharmacy Application Software Services)



Home

About MedSafe

Links

FAQ

Training



Welcome!

VA ADERS (new) - [Launch](#) The VA ADERS program has been updated to include new features as well as to overcome connection and performance limitations related to Java updates. This version is available to any reporters that would like to start using it. The updated version is available here: VA ADERS (new) – [Launch](#) or at the left from the menu option VA ADERS (new) – [Launch](#).

1. Click Accept
2. Select VISN
3. Select Station/Facility
4. Select VA ADERS ajax
5. Click Connect to Site
6. Enter VistA/CPRS Access/Verify code pair

Major Enhancements:

1. Drug look-ups in the primary/secondary suspect drug look-up fields and the treatment medication fields have been modified to provide higher matching rates.
2. Fax Utility – a separate window will open allowing report look-up to check fax status and also a new option to fax up to 10 reports at one time to FDA MedWatch.

Note: The DVBA CAPRI GUI option is available for VA ADERS (new) and VA ADERS (old). [Click here](#) for more information.

For instructions on how to check if you have DVBA CAPRI GUI, click [here](#). If you don't have it, please contact your local ADPAC or local IT.

Please use the option to notify the VA ADERS Staff if you experience a problem.

Software Tools

VA Section 508 Home

VA ADERS - [Overview](#)

VA ADERS (new) - [Launch](#)

VA ADERS (old) - [Launch](#)

MUET - [Overview](#)

MUET - [Launch](#)

NCPS - [Website](#)

Alerts & Notices

MedWatch Alerts

MedSAFE Newsletter

Select "MUET – Launch" to access the application and login



MedSafe Portal

Department of Veterans Affairs
PBM MedSafe
C.P.A.S.S.
Clinical Pharmacy Application Services

Contact Info

Client Settings

Email MUET Staff



Email Staff for HELP!!!

MUET - VA Medication Use Evaluation Tracker 2.10 (Prior Authorization)

NOTICE!

This system is intended to be used by [authorized VA network users] for viewing and retrieving information only except as otherwise explicitly authorized. VA information resides on and transmits through computer systems and networks funded by VA; all use is considered to be understanding and acceptance that there is no reasonable expectation of privacy for any data or transmissions on Government Intranet or Extranet (non-public) networks or systems. All transactions that occur on this system and all data transmitted through this system are subject to review and action including (but not limited to) monitoring, recording, retrieving, copying, auditing, inspecting, investigating, restricting access, blocking, tracking, disclosing to authorized personnel, or any other authorized actions by all authorized VA and law enforcement personnel. All use of this system constitutes understanding and unconditional acceptance of these terms. Unauthorized attempts or acts to either (1) access, upload, change, or delete information on this system, (2) modify this system, (3) deny access to this system, or (4) accrue resources for unauthorized use on this system are strictly prohibited. Such attempts or acts are subject to action that may result in criminal, civil, or administrative penalties.

Select the button "Accept"



MedSafe Portal

Email MUET Staff



Contact Info ▼
Client Settings ▼

MUET - VA Medication Use Evaluation Tracker 2.10 (Prior Authorization)

Use drop down arrows for VISN, Facility.

Access and Verify codes are the same as used for VistA/CPRS.

Select your facility and login to VistA

VISN 12 - The Great Lakes Health Care System ▼
Hines, IL ▼

Access Code:

Verify Code:

Connected to Hines, IL



Initiative

-- select initiative --

List

Use the drop down arrow to view the initiatives.



Initiative

-- select initiative --

- select initiative --
- ESAs with Trigger Groups Based on HGB
- Glyburide with SrCr >= 2 AND Patient >= 65 years
- Pseudoephedrine Quantity > Limit
- Citalopram Review
- Sevelamer Carbonate Quantity >= 540 tabs/30 day Rx
- Target Specific Oral Anticoagulants**
- Women of Childbearing Age on Warfarin
- Prasugrel or Ticagrelor > 12 months
- Potassium F/U in HF with new MRA Rx

List

Scroll down to the initiative you wish to access. Click on "List" to see the interventions.



Questions ?

