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MEDICATION SAFETY IN SECONDS

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

Helping to achieve safe medication use

MEDICATION SAFETY IN THE HOME—STORAGE AND DISPOSAL

Submitted by: Jeanne Tuttle, R.Ph.

Did you know VA offers free of charge, environmentally safe disposal options to Veterans for their unwanted/unneeded medications? VHA Directive 1114, Controlled Substance Patient Prescription Disposal, defines the requirements required in Federal law for controlled substances; however, the program can be used for any prescription or over-the-counter medication. As of April 1st, Veterans have returned over 74 tones of unwanted/unneeded medications that are destroyed in an environmentally responsible manner, keeping these drugs out of our landfills and waterways. All pharmacies have received mail back envelopes free of charge that can be given to our Veterans and there are over 100 on-site receptacles in place across the system. In addition, a prescription can be entered for a mailback envelope(s) to be sent to the Veteran's home if he/she is unable to come into the medical center. Check with your pharmacy leadership to see which options are available at your medical center.

The President's Commission on Combating Drug Addiction and the Opioid Crisis highlights the importance of take-back programs and drug disposal, stating "Many misusers of prescription drugs have indicated they received prescriptions from their family and friends' medicine cabinets." In addition, eliminating all unneeded medications from the home can reduce the chance of accidental and intentional poisonings as well as medication adverse events. The CDC's Medication Safety Program website states "It is estimated that more than 1 million individuals are seen in hospital emergency departments for adverse drug events each year in the United States. Over one-quarter of these patients need to be hospitalized for further treatment." In regards to children, "An estimated 71,000 children (18 years old or younger) are seen in emergency departments each year because of

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NEWSWORTHY...

from the pbm

- Synthetic Marijuana and Potential Risk for Bleeding – 04/05/2018 - National PBM Bulletin

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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

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from the fda

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NEUROLOGY

FDA warns of serious immune system reaction with seizure and mental health medicine lamotrigine (Lamictal)
4/25/2018

The Food and Drug Administration (FDA) warns that lamotrigine (Lamictal) can cause a rare but serious immune system reaction called hemophagocytic lymphohistiocytosis (HLH). Lamotrigine (Lamictal) is used for the treatment of seizures and bipolar disorder. From December 1994 through September 2017, eight cases worldwide of confirmed or suspected HLH associated with lamotrigine (Lamictal) use in children and adults were reported to FDA and in the medical literature. Two cases occurred in the U.S. and six occurred abroad. Doses ranged from 25 mg every other day to 250 mg once daily. For all cases, symptoms occurred within 24 days of starting lamotrigine treatment and consisted of fever (n=8), thrombocytopenia (n=8), hyperferritinemia (n=8), hypofibrinogenemia (n=5), splenomegaly (n=3), anemia (n=3), hypertriglyceridemia (n=2), low or absent Natural Killer (NK) cells (n=1), and neutropenia (n=1). Of the eight cases:

- All had positive bone marrow biopsies consistent with hemophagocytosis.
- All reported serious outcomes and hospitalization.
- Three reported other serious important medical events.
- Two reported the outcome as being life-threatening.
- One reported death.
- Seven improved after treatment and discontinuation of lamotrigine (Lamictal). Treatment reported included steroids (n=6), intravenous immunoglobulin (n=4), blood products (n=2), and chemotherapy (n=2).
- None reported rechallenge.

FDA recommends that health care professionals:

- Discontinue lamotrigine if HLH or another serious immune-related adverse reaction is suspected and an alternative etiology for the signs and symptoms cannot be established.
    - Early signs and symptoms of HLH such as fever and rash are not specific, and may be confused with other serious immune-related adverse reactions such as Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS).
    - At least 5 of 8 of the following symptoms must be present for a diagnosis of HLH:
        - Fever and rash
        - Enlarged spleen
        - Cytopenias
        - Elevated levels of triglycerides or low blood levels of fibrinogen
        - High levels of blood ferritin
        - Hemophagocytosis identified through bone marrow, spleen, or lymph node biopsy
        - Decreased or absent Natural Killer (NK) Cell activity
        - Elevated blood levels of CD25
    - Advise patients to seek immediate medical attention if they experience symptoms of HLH during lamotrigine treatment.
        - Fever, usually >101°F
        - Enlarged liver; symptoms may include pain, tenderness, or unusual swelling over the liver area in the upper right belly
        - Swollen lymph nodes
        - Skin rashes
        - Yellow skin or eyes
        - Unusual bleeding
        - Nervous system problems, including seizures, trouble walking, difficulty seeing or other visual disturbances.

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NEWSWORTHY...

from the fda

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INFECTIOUS DISEASES

FDA review finds additional data supports the potential for increased long-term risks with antibiotic clarithromycin (Biaxin) in patients with heart disease

2/22/2018

FDA will update clarithromycin's label to warn of an increased mortality risk when used in patients with cardiovascular (CV) disease. This is based on the agency's review of a 10-year follow-up study of a randomized controlled trial that found that a two-week course of clarithromycin increased the risk of cardiovascular death for 3 years, compared with placebo, among patients with stable coronary artery disease. Researchers have not identified a potential reason behind the increased mortality risk. Observational studies examining clarithromycin's effect on patients with or without heart disease offer mixed results. Due to lack of prospective, randomized, and controlled trials with prespecified long-term safety outcome measures following clarithromycin treatment in patients who do not have heart disease and inconsistent results from observational studies, FDA cannot apply findings to patients who do not have heart disease. As such, FDA recommends that health care professionals:

- Weigh the benefits and risks of clarithromycin before prescribing to any patient.
- Consider prescribing other antibiotics for at-risk patients.
- Advise patients with CV disease to seek medical attention immediately if they experience signs and symptoms such as chest pain, shortness of breath, pain or weakness in one part or side of their body, or slurred speech regardless of the medical condition for which they are receiving clarithromycin.

Clarithromycin should only be used when there is a clear clinical indication. Typical uses include upper and lower respiratory tract infections, skin and soft tissue infections and helicobacter pylori infections associated with duodenal ulcers.

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unintentional medication poisonings (excluding recreational drug use). Most of these visits (over 80%) were because an unsupervised child found and consumed the medication without adult supervision."

How many times have you encountered a patient who took a medication they were told to stop, but got confused by the multiple prescriptions bottles in the home and ended up in the emergency department or hospital? Providing a safe disposal option and education on the importance of removing unneeded medications from the home, can help prevent these occurrences. There is a one page flyer on the PBM medication disposal site that you can customize to use in educating our Veterans. On this site you will also find marketing materials and staff education resources. Use these resources to help our Veterans keep the home environment safe!

Helpful Links:

- VHA Directive 1114: https://www.va.gov/vhapublications/ViewPublication.asp?pub_ID=3238
- Examples of SOPs, Staff education, Veteran marketing, etc. https://vaww.cmopnational.va.gov/cmop/PBM/Medication Disposal for Patients
- Information on these services for Veterans, as well as medication safety in the home: https://www.pbm.va.gov/vacenterformedicationsafety/vacenterformedicationsafetyprescriptionsafety.asp
- Public Service Announcement developed in partnership with DoD: https://www.youtube.com/watch?v=77-ZbwhVm4s

Getting the most from our safety surveillance

ADVERSE DRUG EVENT PREVENTABILITY USING VA ADERS: A CASE REPORT

Submitted by: Paul Fina, Pharm.D., PGY-2 Medication Use Safety Resident

Adverse drug event (ADE) reporting in Veterans Affairs (VA) is a key component of the medication safety surveillance process. The VA Adverse Drug Event Reporting System (VA ADERS) allows VA clinicians to report suspected ADEs at all VA facilities. After reports are submitted, the information is reviewed to identify trends and potentially preventable ADEs, which may reveal opportunities for process improvements. Such is the case with the following example of a potentially preventable ADE reported to VA ADERS.

A 71-year old patient reported to the VA emergency department in May due to worsening generalized weakness accompanied by falls, poor appetite, and persistent abdominal pain. The patient's medical history at the time of admission included: HTN, atrial fibrillation, asthma, hyperglycemia, CAD, mitral valve replacement (2001), BPH, gout, rectal adenocarcinoma with resection/colostomy (2012), diverticulosis, anxiety, and COPD. He was admitted to the hospital for bradycardia likely secondary to digoxin toxicity, type II NSTEMI, and acute kidney injury. However, his case was made more complicated for providers due to his dual use of both VA and non-VA providers. He was followed more closely by non-VA providers at times, leaving his known medical history incomplete for VA providers.

His elevated labs upon admission included: SCr = 1.8mg/dl (February - 0.7mg/dl); BUN = 73mg/dL; K = 6.1mmol/L; and serum digoxin concentration = 9ng/mL (February - 1.5ng/mL). In addition to digoxin 0.25mg daily (the primary suspect drug reported) his medication list included: metoprolol tartrate 50mg twice daily, gabapentin 200mg twice daily, triamterene/hydrochlorothiazide 37.5/25mg daily, potassium chloride 20mEQ daily, sertraline 200mg daily, simvastatin 40mg daily, albuterol, lorazepam 0.5mg twice daily as needed, indomethacin 25mg twice daily as needed, and melatonin 6mg at bed time as needed. The patient was treated with Digibind in the emergency room prior to being admitted to the ICU, where digoxin, metoprolol, gabapentin, potassium tablets, and indomethacin were discontinued during the patient's hospital stay. His sertraline dose was also decreased. The patient continued to have asymptomatic bradycardia into the 30's while resting or sleeping, but would have an increase in heart rate into the 70's and 80's with exertion. His serum creatinine improved to 1.2mg/dL at discharge.

While not all ADEs are preventable, the VA ADERS report template allows clinicians to evaluate an event for potential preventability by using nine questions. These questions aid in the identification of factors contributing to the ADE occurrence or potential considerations in the selection, ordering, or monitoring of the medication. If relevant information was available prior to the event occurring, these questions help to isolate where within the medication process that information could have made the most beneficial impact. The nine preventability questions from VA ADERS were answered as follows:

Preventability Questions	Answers
1. Was the drug involved considered appropriate for the patient's clinical condition?	NO
2. Was the dose, route, or frequency of administration appropriate for the patient's age, weight, or disease state?	NO
3. Was required therapeutic drug monitoring or other necessary laboratory test(s) performed?	YES
4. Were adjustments in therapy made based on drug monitoring or available lab results?	YES
5. Was there a history of allergy or previous reactions to the drug or drug class that was severe or would indicate the drug should not be used again?	NO
6. Was a drug interaction involved in the reaction?	NO
7. Was a critical serum drug level (or laboratory monitoring test) documented prior to the reaction or event occurring?	N/A
8. Was poor compliance involved in the reaction (missed dose, late doses)?	NO
9. Was hypercompliance involved in the reaction (taking more than prescribed)?	NO

Discussion

After evaluating the reporter's answers to the 9 preventability questions, questions one, two, and seven indicate this digoxin ADE was possibly preventable. 1) Study results regarding the morbidity and mortality rates of digoxin for atrial fibrillation have been mixed, but there are good appropriate alternatives to digoxin as first line therapy for atrial fibrillation according the NICE guidelines.[2-6] 2) The Beers Criteria, a resource listing potentially inappropriate medication use in older adults, includes digoxin 0.25mg daily, the primary suspect drug.[7] He was also on indomethacin and lorazepam (Beer's Criteria medications), and the patient had worsening kidney function, which may have had synergistic contribution to the patient's hospitalization. 7) Although marked as N/A, the patient last had his serum creatinine and digoxin levels checked in February. The patient then had a dramatic change in his clinical condition in a short period of time. Some of the lessons learned from this case include:

- Each dispensed/prescribed medication should have an appropriate therapeutic indication listed in the patient's chart.
- A patient's medical history is often incomplete. Many patients are co-managed by non-VA providers, poor historians, or lost to follow-up for a period of time.
- A patient's medication regimen should change as their clinical status changes. For example, reduce medication doses

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Getting the most from our safety surveillance

ADVERSE DRUG EVENT PREVENTABILITY USING VA ADERS: A CASE REPORT

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or de-prescribe medications in the elderly when appropriate as renal function continually declines with age.

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