

MEDICATION

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

SAFETY IN SECONDS

Helping to achieve safe medication use

NAN ALERT ADVISES FULL USE OF METRIC UNITS ON DOSAGE CUPS AFTER CONFUSION IN SCALES LEADS TO FATAL EVENT

The National Medication Errors Reporting Program operated by the Institute of Safe Medication Practices (ISMP) recently issued a National Alert Network (NAN) alert that reports a fatal event due to confusion of two dosing scales (drams versus milliliters [mL]) that appeared on a plastic oral liquid dosing cup. In this case, a nurse incorrectly administered 1 dram of morphine sulfate (20 mg/dL) instead of the ordered 1 mL of the medication, as both units are shown on the dosing cup. As 1 dram equates to 3.7 mL, this opioid-naïve patient received close to 75mg of morphine.

According to the alert, multiple national organizations advocate adoption of the metric system (milliliter) as the standard for prescribing and measuring liquid medications. However, dosing devices still use alternative

measurements, such as teaspoonful, dessert-spoonful, tablespoonful, drams, and ounces with abbreviations that may be easily confused (i.e., TSP, TBS). A proposed change in USP <17> will call for an appropriate dosing device (i.e., oral syringe, dosing cup, etc.) to be provided for medication measurement and administration, with volume markings listed in metric units and consistent with the dose instructions on the prescription container label. In the meantime, this alert recommends to:

- Move toward full use of metric dosing.
- Eliminate dosage cups that measure liquids in fluid drams.
- Use oral syringes that measure in mL only for oral liquid medications whenever possible.
- If a dosing cup must be used, it should allow measurement in mL only.

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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.

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NEWSWORTHY...

from the pbm

- Adverse Cardiovascular Thrombotic Events with NSAIDs: FDA Strengthens Warning – 08/04/2015 - [National PBM Bulletin](#)
- Ketorolac Recall Due to Particles in Glass Vial: ADDENDUM – 07/02/2015 - [National PBM Patient Level Recall Communication](#)
- Nexium Recall Due to Bottle Containing Seroquel Instead – 06/24/2015 - [National PBM Patient Level Recall Communication](#)

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from the fda

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NEUROLOGY

[FDA warns about cases of rare brain infection with MS drug Gilenya \(fingolimod\) in two patients with no prior exposure to immunosuppressant drugs](#)

8/4/2015

FDA warns that a case of definite progressive multifocal leukoencephalopathy (PML) and a case of probable PML have been reported in patients taking fingolimod (Gilenya) for multiple sclerosis (MS) without prior or concurrent exposure to other immunosuppressant drugs. Although asymptomatic, one patient was diagnosed with probable PML based on MRI findings compatible with PML and JC virus detected in the cerebrospinal fluid (CSF). This patient had a 5-year history of multiple sclerosis (MS) which included a relapse that was treated with interferon beta-1a (Rebif) for 10 months. After interferon beta-1a (Rebif) was discontinued, the patient took (fingolimod) Gilenya for approximately 4 years. In addition, this patient took short-term corticosteroids before and during (fingolimod) Gilenya treatment, but had not received natalizumab (Tysabri) or other drugs known to suppress immune function. The other patient (13-14 year history of MS) was diagnosed with definite PML (based on characteristic symptoms, MRI findings, and JC virus in the CSF) after taking fingolimod (Gilenya) for 2.5 years. Fingolimod (Gilenya) treatment was stopped in both patients. The *Warnings and Precautions* and *Patient Counseling Information* sections of the drug label, as well as the patient Medication Guide, reflects this new information. FDA recommends that health care professionals:

- Be aware that MRI signs of PML may be apparent before clinical symptoms develop.
- Recognize that symptoms are diverse, progress over days to weeks, and can lead to severe disability or death.
- Discuss symptoms of PML with patients receiving fingolimod (Gilenya) treatment for MS, specifically:
 - Symptoms can include the following:
 - progressive weakness on one side of the body or clumsiness of limbs;
 - disturbance of vision;
 - changes in thinking, memory, and or orientation;
 - confusion or changes in personality.
 - Instruct patients to notify their health care provider if they develop any symptoms suggestive of PML.
- Stop fingolimod (Gilenya) immediately at the first sign or symptom suggestive of PML and perform an appropriate diagnostic evaluation.

PML associated with fingolimod (Gilenya) use has been previously discussed in the [Issue 8; Volume 3; September 2013](#) edition of this newsletter.

LOOK-ALIKE SOUND-ALIKE NAME CONFUSION

[FDA warns about prescribing and dispensing errors resulting from brand name confusion with antidepressant Brintellix \(vortioxetine\) and antiplatelet Brilinta \(ticagrelor\)](#)

7/30/2015

As of June 2015, FDA has received 50 medication error reports describing brand name confusion with Brintellix (vortioxetine) and Brilinta (ticagrelor), of which 12 involved wrong prescriptions that were actually dispensed. In most cases, Brintellix was mistaken as Brilinta. Factors contributing to the name confusion may include:

- Both brand names look and sound similar due to beginning with the same three letters.
- Both brand names are presented in close proximity when selecting medications in a computerized physician order entry (CPOE) system.
- The pharmacist was not familiar with the new medication Brintellix and so dispensed Brilinta.

This issue was previously addressed last year in the [Issue 6; Volume 4; June 2014](#) issue of this newsletter, along with recommendations for considerations that pharmacy may take within the VA's computerized provider order entry system to reduce the potential for confusion with these look-alike names.

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from the fda

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CONTRAST AGENTS

[FDA evaluates the risk of brain deposits with repeated use of gadolinium-based contrast agents for magnetic resonance imaging \(MRI\)](#)

7/27/2015

Recent publications in the medical literature have reported that:

- Deposits of gadolinium-based contrast agents (GBCAs) remain in the brains of some patients who undergo four or more contrast magnetic resonance imaging (MRI) scans;
- Trace amounts of gadolinium may stay in the body long-term; and
- Although GBCAs are mostly eliminated from the body through the kidneys, human and animal studies have confirmed that gadolinium can remain in the brain, even in individuals with normal kidney function.
- Available information does not identify any adverse health effects.

FDA does not require manufacturers to make changes to the labels of GBCA products and will study this possible safety risk further with its National Center for Toxicological Research (NCTR), the research community, as well as industry. To reduce the potential for gadolinium accumulation FDA recommends that providers should:

- Consider limiting GBCA use to clinical circumstances in which the additional information provided by the contrast is necessary; and
- Reassess the necessity of repetitive GBCA MRIs in established treatment protocols.

RESPIRATORY

[FDA warns about a serious lung condition in infants and newborns treated with Proglycem \(diazoxide\)](#)

7/16/2015

Eleven cases of pulmonary hypertension (seven cases identified in FAERS from May 28, 1973 [the date of approval] through March 11, 2015, and four cases identified in the medical literature) have been associated with diazoxide (Proglycem). These cases either resolved or improved when diazoxide (Proglycem) was discontinued. FDA recommends that health care providers monitor patients, especially those with risk factors for pulmonary hypertension, for signs of respiratory distress, including tachypnea, flaring nostrils, grunting, and chest wall retractions. Other signs can include feeding intolerance and cyanosis. Common risk factors for pulmonary hypertension include meconium aspiration syndrome, respiratory distress syndrome, transient tachypnea of the newborn, pneumonia, sepsis, congenital diaphragmatic hernia, and congenital heart disease. Discontinue diazoxide (Proglycem) if pulmonary hypertension is identified.

PAIN MANAGEMENT

[FDA strengthens warning that non-aspirin nonsteroidal anti-inflammatory drugs \(NSAIDs\) can cause heart attacks or strokes](#)

7/9/2015

FDA strengthens the warning that nonsteroidal anti-inflammatory drugs (NSAIDs) may be associated with an increased risk of serious and potentially fatal cardiovascular thrombotic events, including myocardial infarction and stroke. Updates to labels of all prescription NSAIDs will reflect new safety information on prescription and OTC NSAIDs based on findings from observational studies, a large combined analysis of clinical trials, other scientific publications, and discussions at a recent Arthritis Advisory Committee and Drug Safety and Risk Management Advisory Committee. FDA recommends that health care providers:

- *Prescribe the lowest effective dose for the shortest duration possible to minimize the risk for an adverse cardiovascular event in patients treated with an NSAID.*
- *Recognize that some NSAIDs, including those in OTC products such as ibuprofen and naproxen, can interfere with the antiplatelet action of low dose aspirin used for cardiovascular protection by blocking aspirin's irreversible COX-1 inhibition.*
- *Remain alert for the development of cardiovascular adverse events throughout the patient's entire treatment course, even in the absence of previous cardiovascular symptoms.*

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- Discuss with patients the risk versus benefits of prescription NSAIDs and over-the-counter (OTC) NSAIDs.
- Inform patients to seek medical attention immediately if they experience symptoms of heart attack or stroke such as chest pain, shortness of breath or trouble breathing, sudden weakness or numbness in one part or side of the body, or sudden slurred speech.

Further details can be found in a [National PBM Bulletin](#) issued earlier this month.

[FDA will evaluate the potential risks of using codeine cough-and-cold medicines in children](#)

7/1/2015

FDA will evaluate the risks of using codeine-containing medications to treat coughs and colds in children less than 18 years of age due to the potential for serious side effects such as respiratory depression. In 2013, FDA cautioned against using codeine products in children with recent tonsillectomy/adenoidectomy because of increased risk of respiratory problems in this group of patients. In April 2015, the European Medicines Agency (EMA) advised not to use codeine to treat cough and cold in children under 12 years of age as well as in children and adolescents between 12-18 years of age who have compromised breathing, including those with asthma or other chronic respiratory conditions. FDA will convene a public advisory committee meeting to discuss these safety issues and any actions, if needed.

CENTRAL NERVOUS SYSTEM

[FDA reports permanent skin color changes associated with use of Daytrana patch \(methylphenidate transdermal system\) for treating ADHD](#)

6/24/2015

FDA warns of acquired skin depigmentation or hypopigmentation consistent with chemical leukoderma associated with the use of the methylphenidate transdermal system (Daytrana patch) for the treatment of Attention Deficit Hyperactivity Disorder (ADHD). FDA added a new warning to the drug label regarding the risk of permanent loss of skin color. This is based on 51 postmarketing reports to the FDA Adverse Event Reporting System (FAERS) from 2006-2014 as well as 1 case report in the medical literature that describe a decrease or loss of pigmentation in skin up to 8 inches in diameter at application sites of the Daytrana patch. Seven of the 51 FAERS cases indicated that areas other than the application site were also affected. Time to onset of leukoderma after initiating treatment with the patch ranged from 2 months to 4 years. Thirteen cases stated use of medications to reverse the loss of skin color, of which 3 indicated a slight improvement. Three cases reported persistent local or distal leukoderma after stopping use of the patch. In all cases, the decreased skin color was permanent. FDA recommends that health care providers should:

- Discontinue the Daytrana patch if loss of pigmentation occurs and consider other long-acting treatment options for ADHD.
- Advise patients or their care givers to monitor for signs of skin depigmentation or hypopigmentation while on treatment and to report any changes in skin color to their health care professionals.

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- Some suppliers can customize dosing cups to measure in mL only. If not available, use cups that measure in mL or household measures until mL-only cups can be supplied.
- Purchase dosing cups that have printed (not embossed) measurement scales for ease of reading.

Further details regarding this alert are available at the following link: <http://www.nccmerp.org/sites/default/files/nan-alert-june-2015.pdf>

REFERENCES:

NAN ALERT. Move toward full use of metric dosing: eliminate dosage cups that measure liquids in fluid drams. Use cups that measure mL. National Coordinating Council on Medication Error Reporting and Prevention (NCCMERP): June 30, 2015.

Getting the most from our safety surveillance

ATTENTION PHARMACISTS: CENTRALLY-AGGREGATED MEDICATION UTILIZATION EVALUATION (CAMUE) - A NEW APPROACH FOR PARTICIPATION IN MULTI-SITE PROJECTS

Submitted by Muriel Burk, Pharm.D. and Madeline McCarren, Ph.D., MPH

The purpose of the Centrally-Aggregated Medication Utilization Evaluation (CAMUE) initiative is to provide VA medical centers (VAMCs) with a “ready-to-use” Medication Utilization Evaluation (MUE) toolkit consisting of a protocol, Access database (with an individual patient data entry form and automated report analysis), and an online template (Infopath form) for submitting aggregate results centrally. Unlike the conventional national multi-site MUE whereby PBM VAMedSAFE collaborated with local VAMCs in the collection of patient-specific data for analysis, CAMUE provides the local VAMC with the tools necessary to conduct and analyze the entire MUE at the site level. After completion at the local level, the online Infopath template is to be used for individual sites to share local results in aggregate with PBM VAMedSAFE. This allows PBM VAMedSAFE to consolidate multiple site-based MUE results in order to assess prescribing patterns for quality assurance and improvement across VA in a manner not unlike a meta-analysis. The use of a uniform protocol and data collection tool will allow for a standardized approach and comparability of results from multiple VAMCs. Individual site data will not be identified in the final national report, but participating sites will be acknowledged. No patient-level data or identifiers are to be shared with VAMedSAFE.

The first CAMUE project will focus on chronic opioid use:

Registration start for the first project: July 2015; See protocol and Excel registration form at VAMedSAFE Sharepoint: <https://vaww.cmopnational.va.gov/CR/VAMedSAFEMultiSiteResearch/camue/default.aspx>

Email the registration form (with email addresses of all who will require access to the data collection tools) to madeline.mccarren@va.gov

Registration close: October 2015 or @ 15 participating sites, whichever occurs first

Toolkit available: August 2015, on VAMedSAFE Sharepoint

Workload: 100 patients reviewed; see protocol for data elements

Target population: Chronic opioid use per OSI Dashboard definition (≥ 90 days)

Due date: Aggregate data are due at VAMedSAFE by November 30, 2015.

More projects utilizing this framework will be introduced later this year. Details to follow. ■