VA Center for Medication Safety

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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

NAN ALERT: POTENTIAL FOR WRONG ROUTE ERRORS WITH EXPAREL® (BUPIVICAINE LIPOSOME INJECTABLE SUSPENSION)

The National Alert Network (NAN), a coalition of members of the National Coordinating Council on Medication Error Reporting and Prevention (NCCMERP), issued an alert addressing the potential for wrong route errors with Exparel® (bupivacaine liposome injectable suspension). Exparel® is a local anesthetic applied topically to a surgical wound at the time of procedure in order to achieve post-operative analgesia. Propofol® is an intravenously administered anesthetic and sedative used during surgical procedures and to facilitate mechanical ventilation. Inadvertent systemic delivery of Exparel® via intravenous administration instead of Propofol® may lead to depressed cardiac conductivity, atrioventricular block, ventricular arrhythmias, and cardiac arrest.

The confusion stems from similar product features between Exparel® and Propofol®:

- Both appear as milky white substances;
- Both have similar packaging that displays teal and white labeling, with greater resemblance in the 20mL vials of Exparel®;
- Use of both occurs in the surgical setting; and
- When prepared in syringes, both look identical, especially if syringes do not have any labeling.

Neither the Institute for Safe Medication Practices (ISMP) nor the Food and Drug Administration (FDA) has received any reports of look-alike medication errors with Exparel® or Propofol®. The alert suggests the following recommendations to help prevent the potential for this mix-up:

- Store/stock Exparel® and Propofol® vials in separate designated areas within the pharmacy or other clinical setting of use.
- Label any prepared syringe or solution, even if intended for immediate administration or infiltration into a surgical site.
- Establish procedures to confirm that any syringe containing unused medication (i.e., Exparel®) never leaves the sterile field without a label.
- Hospitals should provide sterile labels for use when preparing medications in syringes.
- Discard contents of any unlabeled syringe immediately.
- Educate healthcare staff of the potential for wrong route errors with Exparel®, especially those that work in surgical settings (i.e., operating room nurses, pharmacists, anesthesia staff, and surgeons).
- Ensure readily available directions for treatment of bupivicaine toxicity in all surgical areas where Exparel® may be used.

For more information on this NAN alert, visit: www.ismp.org/NAN/files/NAN-20120318.pdf

REFERENCES:

NAN ALERT. Potential for wrong route errors with Exparel (bupivacaine liposome injectable suspension). National Coordinating Council on Medication Error Reporting and Prevention (NCCMERP): March 20, 2012.

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NEWS YOU CAN USE

FROM THE FOOD AND DRUG ADMINISTRATION (FDA)

Revised recommendations for Celexa (citalopram hydrobromide) related to a potential risk of abnormal heart rhythms with high doses
03/28/2012 **(***UPDATE FROM 08/24/2011***)**

New changes have been made to the citalopram product label, specifically:

- ECG and/or electrolyte monitoring should be performed in patients prescribed citalopram who have relative contraindications to citalopram use, such as in those with comorbid conditions predisposing a risk of QT prolongation;
- Previous label recommendations that "contraindicated" citalopram use in patients with congenital QT syndrome because of the risk for QT prolongation have been changed to less stringent terminology of "not recommended" to recognize patients with this condition who could benefit from citalopram or who cannot tolerate other alternatives;
- The maximum dose of citalopram remains at 20mg/day for patients greater than the age of 60 years;
- Citalopram should be discontinued in patients with QTc measurements persistently above 500ms.

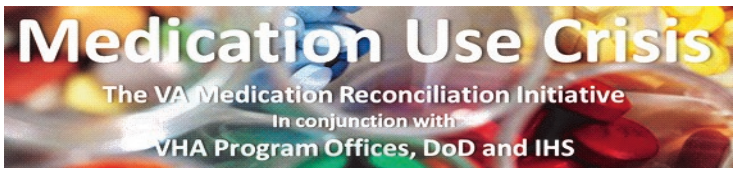
Interactions between certain HIV or hepatitis C drugs and cholesterol-lowering statin drugs can increase the risk of muscle injury
03/01/2012

The FDA has announced labeling revisions for the statin class of lipid-lowering drugs and the protease inhibitor class of drugs used in the management of human immunodeficiency virus (HIV) or hepatitis C virus (HCV). The labeling changes pertain to concurrent use of statins and protease inhibitors and include new recommendations for: 1) statin dose limits, 2) statins to be avoided, or 3) statins that are contraindicated for use in patients receiving HIV or HCV protease inhibitors. The combination of statins and HIV or HCV protease inhibitors can lead to reduced statin metabolism, higher statin serum concentrations and an increased risk for muscle toxicity/injury from statins, including rhabdomyolysis. The changes are as follows:

STATIN	INTERACTING PROTEASE INHIBITOR	PRESCRIBING DETAILS
Atorvastatin	Tipranavir + Ritonavir Telapravir	Avoid atorvastatin
Atorvastatin	Lopinavir + Ritonavir	Use with caution and use the lowest necessary dose of atorva
Atorvastatin	Darunavir + Ritonavir Fosamprenavir Fosamprenavir + Ritonavir Saquinavir + Ritonavir	Do not exceed 20 mg daily of atorvastatin
Atorvastatin	Nelfinavir	Do not exceed 40 mg daily of atorvastatin
Fluvastatin	------	No data available
Lovastatin	HIV protease inhibitors Boceprevir Telapravir	Contraindicated (lovastatin)
Pitavastatin	Atazanavir +/- Ritonavir Darunavir + Ritonavir Lopinavir + Ritonavir	No pitavastatin dose limitations
Pravastatin	Atazanavir +/- Ritonavir Lopinavir + Ritonavir	No pravastatin dose limitations
Rosuvastatin	Atazanavir +/- Ritonavir Lopinavir + Ritonavir	Limit rosuvastatin dose to 10 mg daily
Simvastatin	HIV Protease Inhibitors Bocepravir Telapravir	Contraindicated (simvastatin)

The Statin Criteria for Use have been updated to reflect these changes. VA MedSAFE recommends that facilities continue to report adverse events related to statins or other medications to the VA Adverse Drug Event Reporting System (VA ADERS) as well as to the FDA's Adverse Event Reporting System (AERS-MedWatch). Use of these adverse event-reporting systems helps the VA and FDA observe for trends in adverse events and may help detect safety signals after a drug is marketed.

Contributed by Cathy Kelley, Pharm.D.



VIRTUAL SERIES | May 1, May 8, May 15, & May 22, 2012 | 12:00-4:00PM ET

Background

Medication Use Crisis is described as rampant medication misadventure —Too much, too little, not the right meds for a particular person, adverse drug events at the Veterans home, within Veterans Health Administration (VHA) facilities, and at other federal agencies.

Cost

- The U.S. healthcare system currently incurs more than $177 billion annually in mostly avoidable health costs to treat adverse drug events from the inappropriate use of medications.
- The treatment of chronic disease costs our health system $1.3 trillion annually - about 75 cents of every healthcare dollar.

Solutions

This series of virtual conferences will help close the Medication Use Crisis knowledge gap by providing information to, and sharing experiences with, physicians, nurses, pharmacists and other members of the Federal healthcare community including Department of Defense and Indian Health Services.

These virtual conferences focus on four specific areas or "tracks":

- The Veteran and the Caregiver
- Optimizing Resources
- Teams and Transitions
- Information Management

Why should I register?

By working collaboratively, healthcare teams can join together to help Veterans and their caregivers better understand their medications and how to get the full benefit of their medication therapy, improve therapeutic outcomes, reduce medication errors and adverse drug events and enhance coordination of patient centered care to improve our Veterans' quality of life, and reduce overall healthcare costs.

Gather your colleagues to view and listen to these presentations together at your facility!

Continuing Education Credit

The following Continuing Education Credit has been approved:

- ACCME/ACCME-NP
- ANCC
- APA
- ACPE

Attendees must complete an evaluation at the conclusion of the individual session to receive credit.

How do I sign up?

VA participants – Register through VA TMS by clicking this link: **Medication Use Crisis Conference** . Registration links are contained in the GENERAL INFORMATION folder.

FOR MORE INFORMATION CONTACT:

rosemary.grealish@va.gov or maureen.layden@va.gov

Getting the most from our safety surveillance

METFORMIN AND LACTIC ACIDOSIS

Metformin, a biguanide oral hypoglycemic agent, decreases hepatic gluconeogenesis and also facilitates anaerobic breakdown of glucose into lactate. Lactic acidosis develops whenever production of lactate exceeds its utilization, and is a rare side effect of metformin therapy, occurring with an incidence of about 3 per 100,000 patient-years and an estimated mortality rate of 50%. Metformin-associated lactic acidosis results when pH < 7.35 and blood lactate > 5 mmol. Risk factors for developing metformin-associated lactic acidosis may include conditions that can promote hypovolemia and/or hypoxia (such as cardiovascular and pulmonary dysfunction); decreased lactate clearance (such as hepatic dysfunction and alcohol abuse); and accumulation of metformin (such as acute renal impairment). The signs and symptoms of metformin-induced lactic acidosis include nausea, vomiting, anorexia, epigastric pain, diarrhea, thirst, lethargy, somnolence, and hyperpnea. Therapeutic management of lactic acidosis consists of discontinuing metformin and initiating supportive care, with a focus on hemodialysis and hemofiltration to remove excess lactate and metformin, enhance renal blood flow, restore blood volume, and correct metabolic acidosis. Prevention of metformin-associated lactic acidosis includes awareness of precautions and contraindications for metformin use, as well as the symptoms and risk factors for developing lactic acidosis (i.e., acute kidney failure, dehydration, infection, and use of certain medications that can cause a decline in renal function such as ACE inhibitors, NSAIDS, and intravenous administration of iodinated contrast agents).

Within the VA nation-wide, a review of VA Adverse Drug Event Reporting System (VA ADERS) reports from March 2006 until end of March 2012 involving the primary suspect medication of metformin, or a combination product that contains metformin, showed 6408 reaction symptoms reported from a total of 4930 submissions. Of these, only 81 reported symptoms documented a type of acidosis (Table 1). All have occurred with metformin (no combination products).

Overall, hospitalization for lactic acidosis ensued in 21 patients, and one patient had an outcome of death. In the fatal case, the patient was taking metformin as an outpatient for diabetes. The patient presented to the VA medical center for an aortic valve replacement. Per patient`s wife, patient stopped taking metfomin either the night prior to procedure or the morning of procedure. Patient developed lactic acidosis with lactate level of 25.7 mmol the day after surgery, then 33.1 mmol and 30.7 mmol, respectively, two days post procedure. Patient required vasopressors and bicarb, and developed organ dysfunction. Patient died 3 days post-procedure after full code.

REFERENCES:

1. Lalau JD. Lactic acidosis induced by metformin: Incidence, management and prevention. Drug Saf 2010; 33 (9): 727-740.
2. Salpeter SR, Greyber E, Pasternak GA, Salpeter EE. Risk of fatal and nonfatal lactic acidosis with metformin use in type 2 diabetes mellitus. Arch Intern Med 2003; 163: 2594-2602.
3. Gan SC, Barr J, Arieff AI, Pearl RG. Biguanide-associated lactic acidosis: Case report and review of literature. Arch Intern Med 1992; 152: 2333-2336.
4. Kumar A, Nugent K, Kalakunja A, Pirtle F. Severe acidosis in a patient with type 2 diabetes mellitus, hypertension, and renal failure. Chest 2003; 123: 1726-1729.
5. Glucophage® (metformin hydrochloride), Glucophage XR® (metformin hydrochloride extended release) [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; January 2009.
6. Internal data.

Contributed by: Von Moore, Pharm.D. and Marie Sales, Pharm.D.

TABLE 1. SYMPTOM OF REACTION* TO METFORMIN BY SEVERITY (*MedDRA v15.0 Preferred Term)

	ACIDOSIS HYPERCHLOREMIC	LACTIC ACIDOSIS	METABOLIC ACIDOSIS	ACIDOSIS
MILD		16	1	8
MODERATE	1	20	5	5
SEVERE		18	6	1
TOTAL SYMPTOMS	1	54	12	14

PROVIDER RECOMMENDATIONS FOR ADVERSE EVENT REPORTING:

- Providers should continue to report any adverse events with metformin by entering the information into CPRS' Allergies/ Adverse Reactions field and via local reporting mechanisms. Facilities should continue to report adverse events into VA ADERS and from VA ADERS to the FDA (as appropriate).
- **For VA ADERS Reporting:** When reporting an event that has multiple factors involved such as metformin-associated lactic acidosis, ensure that the report contains the information that describes the event to the fullest detail by using tabs 4, 5, and 6 in VA ADERS as follows.
  - Select the option to report an FDA MedWatch report.
  - **Tab 4 Outcomes**: The optional narrative may be completed with a summary of the event.
  - **Tab 5 Event Section #1:** Mark the Other box and enter the symptoms that are appropriate - "lactic acidosis, lactate level increased".
  - **Tab 6 Event Section #2:** Include the relevant tests/labs and any other relevant history. This section can be used to evaluate the individual event for contributing factors of the event.