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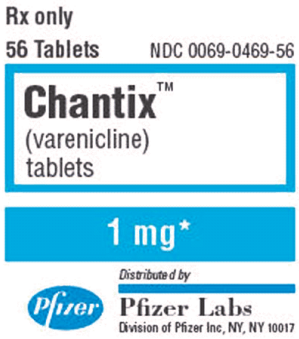
Medication safety in seconds

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

Helping to achieve safe medication use

VARENICLINE (CHANTIX®) AND NEUROPSYCHIATRIC HOSPITALIZATIONS SAFETY REVIEW UPDATE

The U.S. Food and Drug Administration (FDA) sponsored two epidemiological studies – a Department of Veterans Affairs' (VA) Center for Medication Safety (VAMedSAFE) study and a Department of Defense (DoD) study. Both studies evaluated the risk of neuropsychiatric hospitalizations associated with the smoking cessation drug varenicline (Chantix®) , and each resulted in no difference between varenicline (Chantix®) and nicotine replacement therapy (NRT; e.g., NicoDerm patches). Nonetheless, the results do not preclude the increased risk of ANY neuropsychiatric event with varenicline (Chantix®) due to study design limitations:



- Small sample size did not allow power to detect rare events;
- Adverse outcomes without the need for hospitalizations did not get captured;
- VA did not assess PTSD in their outcomes, although evidence suggests increased neuropsychiatric adverse effects when patients with PTSD use varenicline;
- DoD did not evaluate the rate of neuropsychiatric hospitalizations occurring over a longer duration following a varenicline (Chantix®) prescription fill.

Since the above results are preliminary and pending further analyses, VA providers must continue to assess past medical and psychiatric history, specifically suicidality, when considering use of varenicline (Chantix®). As additional safety information on varenicline (Chantix®) becomes available, guidance and Criteria for Use (Varenicline Criteria for Prescribing) will be updated accordingly. The manufacturer of varenicline (Chantix®), Pfizer, continues to assess neuropsychiatric adverse events via a large safety clinical trial with results expected in 2017.

REFERENCES

1. FDA Drug Safety Communication – Safety review update of Chantix (Varenicline) and risk of neuropsychiatric adverse events. http://www.fda.gov/Drugs/DrugSafety/ucm276737.htm . (Accessed 10/24/11).

NEWS YOU CAN USE

FROM THE VA NATIONAL PBM: BULLETINS, COMMUNICATIONS, & RECALLS

- Citalopram Hydrobromide (Celexa®) and Dose-Dependent QT Interval Prolongation: UPDATE - National PBM Bulletin – 09-29-2011
- Oral Contraceptives and Packaging Error Recall - National PBM Communication – 09-21-2011

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NEWS YOU CAN USE

FROM THE FOOD AND DRUG ADMINISTRATION (FDA)

Drospirenone - Safety review update on the possible increased risk of blood clots with birth control pills containing drospirenone
9/26/2011
Epidemiologic studies, including one FDA-funded study, have evaluated the risk of blood clots (venous thromboembolism, VTE) in women using birth control pills containing drospirenone compared to products containing levonorgestrel or other progestins. Conflicting findings range from no difference to as high as 3-fold greater risk of blood clots in women using oral contraceptives containing drospirenone. Doses studied include 3 mg of drospirenone with 0.03 mg of ethinyl estradiol (an estrogen). Risk of drospirenone-containing products with a lower dose of estrogen (e.g., 0.02 mg ethinyl estradiol) remain unknown. Factors for increased risk of VTE in users of birth control pills include smoking, obesity, and family history of VTE, in addition to other factors that contraindicate use of combination oral contraceptives. Providers should caution women currently using a drospirenone-containing birth control pill of the potential risk for blood clots.

Zofran (ondansetron) - Abnormal heart rhythms may be associated with use of Zofran (ondansetron)
9/15/2011
QT prolongation is an existing cardiovascular concern with ondansetron as reflected in the product labeling as well as in medical literature. FDA requested a new warning to avoid the use of ondansetron in patients with congenital long QT syndrome due to risk for developing Torsade de Pointes. Revised labeling will contain this updated warning as well as additional recommendations for ECG monitoring in patients with electrolyte abnormalities (e.g., hypokalemia or hypomagnesemia), congestive heart failure, bradyarrhythmias, or in patients taking other medications that can lead to QT prolongation. GlaxoSmithKline will conduct a thorough QT study to determine the degree to which Zofran (ondansetron) may cause QT interval prolongation, with results expected in summer 2012.

Tumor Necrosis Factor-alpha - Drug labels for the Tumor Necrosis Factor-alpha (TNFα) blockers now include warnings about infection with Legionella and Listeria bacteria
9/7/2011
Updated Boxed Warnings for all Tumor Necrosis Factor-alpha (TNFα) blockers now include the risk of infection from two bacterial pathogens, Legionella and Listeria monocytogenes. FDA received case reports of infections involving both pathogens with some fatalities documented. The medical literature also describes Legionella and Listeria infections resulting in some fatalities in patients taking TNFα blockers, and in some instances, concomitant immunosuppressive drugs.

Saphris (asenapine maleate) - Serious allergic reactions reported with the use of Saphris (asenapine maleate)
9/1/2011
FDA's Adverse Event Reporting System (AERS) database received 52 cases of Type I hypersensitivity reactions (allergic reactions) with the use of the antipsychotic medication Saphris (asenapine maleate). Symptoms included: anaphylaxis, angioedema, hypotension, tachycardia, swollen tongue, dyspnea, wheezing, and rash. Of the 52 cases, 15 reported resolution of symptoms following Saphris discontinuation (of which 2 reported a reappearance of symptoms upon rechallenge); 19 cases resulted in hospitalization or emergency room visits; and 7 required therapeutic interventions. Revised product labeling reflects this risk.

Reclast (zoledronic acid) - New contraindication and updated warning on kidney impairment for Reclast (zoledronic acid)
9/1/2011
Current product information addresses renal toxicity with use of Reclast (zoledronic acid) and dose reductions for patients with renal impairment. A January 2009 FDA post-market safety review identified five deaths from acute renal failure following Reclast infusion, leading to a label revision recommending to monitor serum creatinine before each dose of Reclast. A follow-up review by the FDA in April 2011 showed an additional 11 cases of fatal acute renal failure and 9 cases of renal injury requiring dialysis after Reclast infusion. As a result, new product labeling will now include risk factors for nephrotoxicity with the use of Reclast as well as additional recommendations:

- *Reclast is contraindicated in patients with creatinine clearance less than 35 mL/min or in patients with evidence of acute renal impairment.*
- *Continue to screen patients prior to each administration of Reclast to identify those with underlying acute or chronic renal impairment, advanced age, or dehydration. Patients with underlying renal impairment appear to be at highest risk for kidney failure. Reclast should be used with caution in this population.*
- *The risk of acute renal failure may increase with underlying renal disease and dehydration secondary to fever, sepsis, gastrointestinal losses, diuretic therapy, etc. The risk of developing renal failure in patients with renal impairment also increases with age.*

FOR MUE AND MUET USERS

UPDATES: ONGOING MEDICATION USE EVALUATIONS (MUEs) AND MEDICATION USE EVALUATION TRACKERS (MUETs)

A Medication Use Evaluation (MUE) is a performance improvement method that focuses on evaluating and improving medication-use processes with the goal of improving patient outcomes. VAMedSAFE has developed a Medication Use Evaluation Tracker (MUET) to facilitate MUE procedures.

- **ESA MUET**

A lower hemoglobin (Hgb) trigger group has been incorporated into the ESA MUET in light of the recent FDA alert and PBM Communication regarding revised dosing recommendations for erythropoiesis-stimulating agents (ESAs) in the treatment of anemia in patients with chronic kidney disease (CKD) following review of additional data on increased risk of cardiovascular (CV) events with higher Hgb targets during ESA therapy. It is important to reiterate that the goal is to use the lowest effective dose of ESA to prevent the need for red blood cell transfusions and to individualize therapy, rather than maintaining a tight Hgb range.

The gradient view of the different Hgb ranges in the MUET table allows sites to direct efforts at priority trigger groups, as well as to observe the distribution of potentially outlying Hgb levels in their ESA patients.

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Getting the most from our safety surveillance

ETIDRONATE AND ETODOLAC | POTENTIAL LOOK-ALIKE (LA)/SOUND-ALIKE (SA) CONFUSION

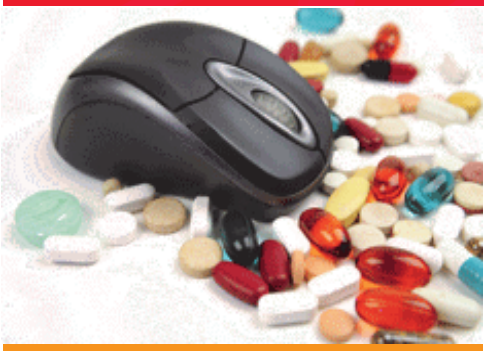
One facility reported an LA/SA error between etodolac and etidronate that involved a provider selection error in CPRS. Typing "*ET*" into CPRS lists the following drug selections in alphabetical order, with ETIDRONATE appearing first and ETODOLAC appearing below. The provider chose the first drug (etidronate) and selected the 200mg dosage. As such, the provider inadvertantly prescribed etidronate 200mg twice daily for knee pain instead of the intended etodolac for knee pain, and the patient subsequently received the wrong medication. A pharmacist identified the error upon renewal for the etidronate 200mg order since the patient had no indication for osteoporosis treatment. A review of the documentation from the clinic visit where this prescription originated uncovered that the order was supposed to be for etodolac. The pharmacist informed the provider and patient. Although the patient took etidronate 200mg twice daily for 30 days prior to the error being identified, no adverse effects were reported by the patient nor noted by the facility provider. As a result, the site evaluated etidronate use at the local level and found one patient who had an appropriate indication and administration schedule. Facility underwent local staff education and the drug message for both medications was updated to warn healthcare providers of the potential for LA/SA confusion.

Etodolac and etidronate is not a medication name pair recognized by the United States Pharmacopoeia (USP) or the Institute for Safe Medication Practices (ISMP) as having the potential for look-alike/sound-alike (LA/SA) confusion. The drug pair also does not appear in First Databank Tallman Lettering. Etidronate prevents and treats osteoporosis in addition to treating other bone conditions such as Paget's disease. Etodolac relieves pain, tenderness, swelling, and stiffness caused by osteoarthritis and rheumatoid arthritis, as well as pain from other causes. Incorrectly receiving etidronate instead of etodolac would subject the patient to suboptimal pain/inflammation control while introducing the risks of GI events, esophagitis and other esophageal events, as well as possible esophageal cancer (conflicting findings exist and FDA continues to evaluate this outcome). On the other hand, patients inadvertently prescribed/administered etodolac instead of etidronate may not get adequate bone loss prevention, leading to breakdown of old bone. Additionally, possible ossification in people who have had total hip replacement surgery or in people who have had an injury to the spinal cord may occur. NSAID-induced gastric bleeding may also become an issue.

REFERENCES

1. Field Information Report.
2. USP Quality Review: Use Caution, Avoid Confusion. Rockville, MD: USP Center for the Advancement of Patient Safety. 79; 2004 April.

PROVIDER RECOMMENDATIONS:



- Consider informing providers of the potential for look-alike/sound-alike confusion between etidronate and etodolac when ordering these medications via the computer order entry system, especially if both medications remain orderable via the alphabetic medication list in CPRS.
- Consider carefully checking the name, dosage, and indication when either etidronate or etodolac is ordered, especially if both medications remain orderable via the alphabetic medication list in CPRS.
- Consider ensuring that a method is in place to help differentiate the products in the computer order entry system to avoid future LA/SA confusion.

FOR MUE AND MUET USERS

UPDATES: ONGOING MEDICATION USE EVALUATIONS (MUEs) AND MEDICATION USE EVALUATION TRACKERS (MUETs)

(continued from page 2)

The following is a screen shot of the ESA MUET trigger groups.

Initiative: ESAs with Trigger Groups Based on HGB

DATA PULL	DATE	NO HGB	MOST RECENT HGB < 9 AND NO FERRITIN	MOST RECENT HGB>11 AND <= 12	MOST RECENT HGB>12 AND <= 13	HGB > 13

- **Citalopram MUET**

PBM in cooperation with other offices in VHA sent out an updated PBM bulletin on the revised maximum dose of citalopram. Patients receiving citalopram at a dose greater than recommended from August 1, 2011 to September 18, 2011 have been loaded to MUET.

- Citalopram average daily dose > 60 mg / day
- Citalopram average daily dose > 40 mg / day
- Citalopram average daily dose > 20 mg / day and age > 60 years
- Citalopram average daily dose > 20 mg / day and prescribed Cimetidine

- **Sevelamer MUET**

Based on discussions at the national MAP-VPE quarterly meeting, the PBM has identified patients receiving > or = 540 sevelamer carbonate 800 mg tablets per 30dayRx (i.e., > or = 14.4 gm/day which is above the maximum studied dose) within the timeframe of 6/2011 through 9/20/2011. This information is available via MUET for follow-up at the local level as deemed appropriate.

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