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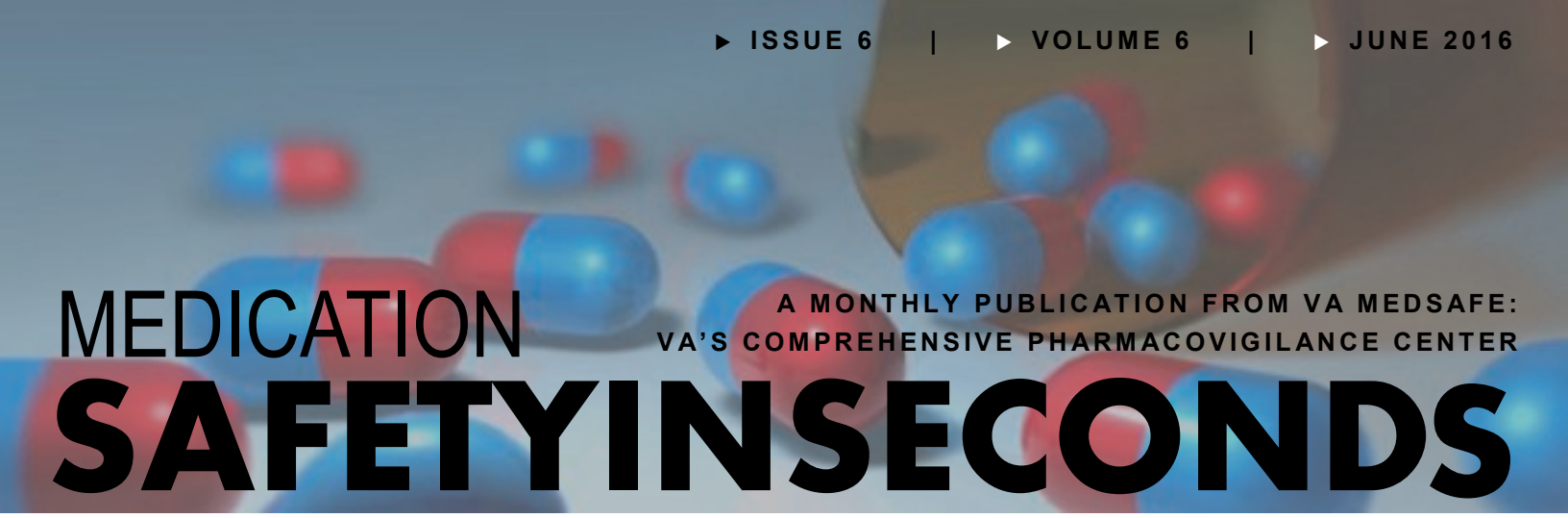

MEDICATION SAFETYINSECONDS

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

Helping to achieve safe medication use

ISMP UPDATES ITS LIST OF DRUG NAME PAIRS WITH TALL MAN LETTERS

Studies suggest that tall man lettering can reduce errors related to look-alike confusion due to drug name similarities, although evidence remains mixed due to methodological differences and significant study limitations. Nevertheless, use of tall man lettering has been endorsed by The Joint Commission (recommended, not required), the US Food and Drug Administration (FDA), the World Health Organization (WHO), and the International Medication Safety Network (IMSN). Further, respondents from a survey conducted by ISMP between February and April 2016 referred to the tall man letters as a "visual alert system" and a "subconscious cue" that help to "refocus the eye" and "slow down or stop the process" to ensure they have the correct drug. They reported that tall man letters serve as a reminder that the drug has been associated with previous look-alike confusion, causing them to pay more attention, read the drug name more carefully, and confirm appropriateness for the patient.

The Institute for Safe Medication Practices' (ISMP) strategy of "tall man" lettering distinguishes the unique characteristics of orthographically similar drug names by enhancing a unique portion of the drug names with upper case letters or by other means such as color, contrasting background, bolding, italicizing, or combinations of the above, in order to reduce the risk of look-alike confusion (i.e, hydr**OXY**zine and hydr**ALAZINE**). To promote standardization in the use and application of tall man letters in health settings, ISMP has maintained a list of drugs names with recommended, bolded tall man letters since 2008. Generic-generic drug name pairs comprise the majority of the list with few brand-brand or brand-generic name pairs included. ISMP follows the CD3 rule to determine which letters to present in upper case. This method

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NEWSWORTHY...

from the pbm

- Fluoroquinolone Safety - 06/03/2016 - National PBM Bulletin
- Ketoconazole Safety - 05/31/2016 - National PBM Bulletin
- Canagliflozin and Risk of Amputations - 05/31/2016 - National PBM Bulletin
- Antipsychotic Agents and Safety Issues - 05/13/2016 - National PBM Bulletin

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IN THIS ISSUE:

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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NEWSWORTHY...

from the fda

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INFECTIOUS DISEASE

FDA warns that prescribing of Nizoral (ketoconazole) oral tablets for unapproved uses including skin and nail infections continues; linked to patient death

5/19/2016

A Food and Drug Administration (FDA) safety review found that oral ketoconazole continues to be prescribed for treatment of skin and nail fungal infections **despite previous label changes limiting usage of ketoconazole (Nizoral) oral tablets due to potentially fatal liver injury and risk of drug interactions as well as adrenal gland problems**.

FDA recommends that:

- Health care professionals should use ketoconazole tablets only to treat serious fungal infections when no other antifungal therapies are available. **It is extremely unusual for ketoconazole to be more appropriate than other antifungal therapies.**
- Since skin and nail fungal infections in otherwise healthy persons are not life-threatening, the risks associated with oral ketoconazole outweigh the benefits.
- Providers should discuss with their patients the risks and benefits of available therapies before using any medicine to treat skin and nail fungal infections.
- Providers should instruct patients taking ketoconazole tablets to seek medical attention right away if they experience any of these signs and symptoms of liver problems, which include loss of appetite, nausea, vomiting, or abdominal discomfort; yellowing of the skin or the whites of the eyes (jaundice); unusual darkening of the urine or lightening of the stools; or pain and discomfort in the right upper abdomen where the liver is located.

For further details, please see the National PBM Bulletin issued last month.

FDA advises restricting fluoroquinolone antibiotic use for certain uncomplicated infections; warns about disabling side effects that can occur together

5/12/2016

An FDA safety review shows that systemic use (i.e. tablets, capsules, and injectables) of fluoroquinolones is associated with disabling and potentially permanent serious side effects involving the tendons, muscles, joints, nerves, and central nervous system that can occur together. This drug class should be reserved for serious infections, and avoided for upper respiratory tract infections (URI) or uncomplicated urinary tract infections (UTI) unless there is a compelling reason. FDA further recommends that:

- Serious side effects associated with fluoroquinolone antibacterial drugs generally outweigh the benefits for patients with acute sinusitis, acute bronchitis, and uncomplicated urinary tract infections (UTI) who have other treatment options.
- For patients with these conditions, fluoroquinolones should be reserved for those who do not have alternative treatment options.
- Providers should instruct patients to contact their health care professional immediately if they experience any serious side effects while taking fluoroquinolone medicine such as tendon, joint and muscle pain; a "pins and needles" tingling or pricking sensation; confusion; and hallucinations.
- Providers should stop systemic fluoroquinolone treatment immediately if a patient reports serious side effects, and switch to a non-fluoroquinolone antibacterial drug to complete the patient's treatment course.

For further details, please see the National PBM Bulletin issued earlier this month.

ENDOCRINOLOGY

Interim clinical trial results find increased risk of leg and foot amputations, mostly affecting the toes, with the diabetes medicine canagliflozin (Invokana, Invokamet); FDA to investigate

5/18/2016

FDA is currently investigating interim safety results from an ongoing clinical trial showing an increase in leg and foot amputations, mostly affecting the toes, in patients treated with canagliflozin (Invokana, Invokamet)

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from the fda

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for diabetes. FDA continues to evaluate this new safety issue and will update the public on whether canagliflozin increases the risk of leg and foot amputations as new data becomes available. In the meantime, FDA recommends that healthcare professionals:

- Monitor patients receiving canagliflozin (Invokana, Invokamet) for any new pain or tenderness, sores or ulcers, or infections in their legs or feet.
- Instruct patients taking canaglifozin to notify their health care professionals right away if they notice any new pain or tenderness, sores or ulcers, or infections in their legs or feet.
- Inform patients not to stop or change their diabetes medicines without first talking to their health care professional because doing so can lead to uncontrolled blood sugar levels that can cause harm.

For further details, please see the National PBM Bulletin issued last month.

CENTRAL NERVOUS SYSTEM

FDA warns about rare but serious skin reactions with mental health drug olanzapine (Zyprexa, Zyprexa Zydis, Zyprexa Relprevv, and Symbyax)

5/10/2016

FDA reports Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) associated with the use of olanzapine (Zyprexa, Zyprexa Zydis, Zyprexa Relprevv, and Symbyax, and generics) and will add a new warning concerning this to the label of all olanzapine-containing drugs. Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) is a potentially fatal drug reaction with a mortality rate of up to 10%. Healthcare professionals should:

- Inform patients about the risk DRESS associated with the use of olanzapine-containing products.
- Explain the signs and symptoms of DRESS to patients and tell them when to seek immediate care if signs and symptoms occur, such as :
  - ◊ Cutaneous reaction (such as rash or exfoliative dermatitis)
  - ◊ Eosinophilia
  - ◊ Fever
  - ◊ Lymphadenopathy
  - ◊ One or more systemic complications such as hepatitis, myocarditis, pericarditis, pancreatitis, nephritis, and pneumonitis
- Instruct patients to not stop taking olanzapine or change their dose without first talking to their health care professional and that sudden stopping of the medicine can be harmful without direct supervision.
- If DRESS is suspected, providers should discontinue olanzapine treatment immediately.
- Since there is currently no specific treatment for DRESS, the important ways to manage DRESS are early recognition of the syndrome, discontinuation of the offending agent as soon as possible, and supportive care. Treatment with systemic corticosteroids should be considered in cases with extensive organ involvement.

For further details, please see the National PBM Bulletin issued last month.

FDA warns about new impulse-control problems associated with mental health drug aripiprazole (Abilify, Abilify Maintena, Aristada)

5/3/2016

FDA reports uncontrollable and excessive urges for gambling, shopping, binge eating and sexual behavior associated with the use of aripiprazole (Abilify, Abilify Maintena, Aristada), an atypical antipsychotic indicated for the treatment of schizophrenia, bipolar disorder, depression (adjunctive treatment), irritability associated with autistic disorder, and Tourette's disorder. Healthcare professionals should:

- Inform patients and caregivers of the risk of impulsive behavior, such as uncontrollable and excessive urges for gambling, shopping, binge eating and sex associated with the use of aripiprazole (Abilify, Abilify Maintena, Aristada).
- Ask patients whether they are experiencing new or increasing urges while receiving this agent.

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NEWSWORTHY...

from the fda

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- Closely monitor for new or worsening uncontrollable urges in patients at higher risk for impulse-control problems, including: those with a personal or family history of obsessive-compulsive disorder, impulse-control disorder, bipolar disorder, impulsive personality, alcoholism, drug abuse, or other addictive behaviors.
- Consider reducing the dose or stopping the medicine if new or increased impulsive or compulsive behaviors develop.

For further details, please see the National PBM Bulletin issued last month.

MISCELLANEOUS

FDA approves brand name change for antidepressant drug Brintellix (vortioxetine) to avoid confusion with antiplatelet drug Brilinta (ticagrelor)

5/2/2016

FDA approved a brand name change for the antidepressant Brintellix (vortioxetine) to decrease the risk of look-alike/sound-alike (LA/SA) errors resulting from name confusion with the blood-thinning medicine Brilinta (ticagrelor). The new brand name of the drug will be Trintellix, and it is expected to be available starting in June 2016. For further details, please see last month's issue of the newsletter available at: Issue 5; Volume 6; May 2016.

Getting the most from our safety surveillance

SAXAGLIPTIN: HEART FAILURE AND HOSPITALIZATION UPDATE

FDA reports that type 2 diabetes medicines containing saxagliptin and alogliptin may increase the risk of heart failure and adds new warnings to the drug labels. This is based on two large clinical trials conducted in patients with type 2 diabetes mellitus as well as heart disease. For details, please see Issue 5; Volume 6; May 2016 .

Interestingly, two observational studies conducted in the US population found that the risk was not increased with saxagliptin relative to sitagliptin. Additional analyses in these studies found that the risk of hospitalization for heart failure was less or comparable to other diabetes drugs (sulfonylureas, thiazolidinediones, insulin). Furthermore, a rapid cycle evaluation conducted in VA data assessed the risk of hospitalization for heart failure in incident user cohorts of saxagliptin or linagliptin compared to sitagliptin. The results of the review found that the risk of hospitalization for heart failure was not increased with saxagliptin or linagliptin relative to sitagliptin. The results in VA patients led to similar conclusions as the previously mentioned observational studies.

REFERENCES:

1. FDA Drug Safety Communication: FDA adds warnings about heart failure risk to labels of type 2 diabetes medicines containing saxagliptin and alogliptin. http://www.fda.gov/Drugs/DrugSafety/ucm486096.htm . Accessed 6/29/2016.
2. Fu AZ, Johnston SS, Ghannam A, et al. Association between hospitalization for heart failure and dipeptidyl peptidase 4 inhibitors in patients with type 2 diabetes: An observational study. *Diabetes Care*. 2016 May; 39(5): 726-34.
3. Toh S, Hampp C, Reichman ME, et al. Risk for hospitalized heart failure among new users of saxagliptin, sitagliptin, and other anithyperglycemic drugs: A retrospective cohort study. *Ann Intern Med*. 2016; 164:705-714.
4. Internal data.

Helping to achieve safe medication use

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suggests moving letter by letter from the left of the drug name towards the right and capitalizing all characters to the right once two or more dissimilar letters are encountered; then, working backwards from the right side of the word towards the left, returning to lower case letters when two or more letters common to both words appear. In the absence of common letters on the right side of the word, the rule suggests capitalizing the central part of the word only. ISMP encourages that the tall man lettering scheme provided by FDA and ISMP be followed for consistency. The current FDA and ISMP lists of Look-Alike Names with Recommended Tall Man Letters can be found on the ISMP website (www.ismp.org/sc?id=1746).

REFERENCES:

Institute for Safe Medication Practices. Special Edition: Tall Man Lettering - ISMP updates its list of drug names with tall man letters. *ISMP Medication Safety Alert! Acute Care*. 21(11): 1-6. June 2, 2016. ■