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MEDICATION SAFETYINSECONDS

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

Helping to achieve safe medication use

CHLORHEXIDINE GLUCONATE ORAL RINSE 0.12% AND LIDOCAINE HYDROCHLORIDE ORAL TOPICAL SOLUTION 2% - POTENTIAL LOOK-ALIKE CONFUSION

The Institute for Safe Medication Practices (ISMP) National Medication Errors Reporting Program (MERP) received 14 reports of look-alike confusion between chlorhexidine gluconate oral rinse 0.12% and lidocaine hydrochloride oral topical solution 2%, both manufactured by Hi-Tech Pharmacal, due to:

- Similar packaging (size, shape) of unit dose containers (Figure 1);
- Similar labels for both products (turquoise printing on white background);
- Small font size;
- Similar display of bar codes on the product label.

Documented mix-ups primarily involved pharmacy dispensing and storage errors. No serious outcomes were reported.

FDA issued a communication earlier this year (that was addressed in a National PBM Bulletin as well as in the Issue 2; Volume 7; February 2017 edition of this newsletter) about rare, but serious allergic reactions, including fatal anaphylaxis that can occur with topical or oral use of chlorhexidine gluconate on an over-the-counter (OTC) or prescribed basis. Inadvertent use of chlorhexidine gluconate may elicit a life-threatening allergic reaction in those with sensitivity to the product. On the other hand, accidental administration of lidocaine may anesthetize the mouth and affect the gag reflex that protects the airway when swallowing.

Since Hi-Tech Pharmacal is currently the only supplier of these items in unit dose cups, ISMP recommends taking steps to avoid confusion such as using auxiliary labels to distinguish between the two products.

REFERENCE

Institute for Safe Medication Practices (ISMP). Safety Briefs: Chlorhexidine mixed up with lidocaine oral solution. *ISMP Medication Safety Alert! Acute Care* February 2017; 22 (3): 1-3.

Figure 1. Similar packaging elements of Hi-Tech Pharmacal's chlorhexidine gluconate rinse and lidocaine oral solution lead to look-alike product confusion reported to ISMP.

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.

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NEWSWORTHY...

from the pbm

- EpiPen and and EpiPen Jr Auto-Injector: Recall - Failure to Activate Device – 04/04/2017 - National PBM Patient Level Recall Communication

from the fda

PAIN MANAGEMENT

FDA restricts use of prescription codeine pain and cough medicines and tramadol pain medicines in children; recommends against use in breastfeeding women
4/20/2017

The Food and Drug Administration (FDA) is restricting the use of codeine and tramadol medicines in children and is requiring several changes to the labels of all prescription medicines containing these drugs, including:

- A *Contraindication* against use of codeine and tramadol for treatment of pain in children younger than 12 years; and also against codeine for use to relieve cough in these children.
- A new *Contraindication* restricting tramadol use in children younger than 18 years to treat pain after a tonsillectomy and/or adenoidectomy. Codeine-containing products already document this Contraindication in product labels.
- A new *Warning* that recommends against the use of codeine and tramadol in adolescents between 12 and 18 years with obesity, obstructive sleep apnea, or compromised respiratory function that may increase the risk of serious breathing problems.
- A stronger *Warning* not to breastfeed during treatment with codeine or tramadol due to the potential for serious adverse reactions in a breastfed infant, such as excess sedation, respiratory depression, and death.

Adverse event reports submitted to FDA from January 1969 to May 2015 identified:

- 64 cases of serious breathing problems, including 24 deaths, with codeine-containing medicines in children younger than 18 years.
- 9 cases of serious breathing problems, including 3 deaths, with the use of tramadol in children younger than 18 years.

Data from medical literature on codeine use during breastfeeding, revealed numerous cases of excess sleepiness and serious breathing problems in breastfed infants, including one death. Although tramadol use during breastfeeding did not reveal any cases of adverse events in the medical literature, tramadol and its active form are also present in breast milk and carry risks associated with ultra-rapid metabolism similar to codeine.

FDA recommends that health care professionals:

- Recognize that all tramadol-containing products and single-ingredient codeine drugs are FDA-approved for use only in adults.
- If a codeine-or tramadol-containing product is appropriate for an adolescent patient:
  - Counsel parents and caregivers on the signs of opioid toxicity (i.e., slow or shallow breathing, difficult or noisy breathing, confusion, or unusual sleepiness); and
  - Advise them to stop giving the adolescent codeine or tramadol and seek medical attention immediately if their adolescent is exhibiting these symptoms.

VA providers should advise patients who receive opioids (including tramadol and codeine-containing medications [such as, but not limited to, cough syrup]) to store these products where they will not be accessible to children and adolescents.

Getting the most from our safety surveillance

BETA-BLOCKERS IN HEART FAILURE WITH REDUCED EJECTION FRACTION (HFrEF)

Submitted by: Elaine Furmaga, Pharm.D.

VA UTILIZATION: Per a recent PBM and VA MedSAFE database evaluation of beta-blocker use in VA, it was noted that approximately 64% of patients with HF*r*EF (estimate per select diagnosis coding) being treated with a beta-blocker were prescribed guideline-concordant beta-blockers.

GUIDELINE RECOMMENDATIONS AND EVIDENCE FOR BETA-BLOCKERS WITH IMPROVED MORTALITY DATA IN PATIENTS WITH HF*r*EF:

- A beta-blocker that has proven to reduce mortality is recommended for patients with current or prior symptoms of HF*r*EF, unless contraindicated, to reduce morbidity and mortality (Class I Recommendation; Level of Evidence A).
- Meta-analyses of beta-blocker trials show a reduction in mortality of approximately 30 to 35%. The beta-blockers that are recommended in HF*r*EF and that have demonstrated a reduction in morbidity and mortality include **bisoprolol, carvedilol, and sustained release metoprolol succinate**. It is unknown if other beta-blockers have a similar benefit, as not all beta-blockers studied have shown a clear reduction in mortality.

COMPARISON OF EVIDENCE-BASED BETA-BLOCKERS FOR HF*r*EF

Beta-Blocker	Bisoprolol	Carvedilol	Metoprolol XL[a]
VA National Formulary	√[b]	√	√[b]
FDA Indication			
Heart Failure		√	√
Angina			√
Post-AMI with LVEF < 40%		√	
Hypertension	√	√	√
$Beta_1$ cardioselective	√		√
Alpha-blocker		√	
Once daily regimen	√		√

AMI=acute myocardial infarction; LVEF=left ventricular ejection fraction
[a] Metoprolol XL=sustained release metoprolol succinate
[b] Restricted to patients with heart failure

APPROXIMATE DOSE EQUIVALENTS OF BETA-BLOCKERS USED IN HF*r*EF

- The beta-blockers **atenolol and immediate-release metoprolol tartrate** have been studied in patients with HF*r*EF; **however, data as to their long-term clinical outcome benefit and optimal dose have not been determined**.
- According to an internal database evaluation, close to 3% of patients prescribed atenolol (~250 to 550 uniques per VISN), and nearly 8% of patients prescribed metoprolol tartrate (~1500 to 4000 uniques per VISN) had a diagnosis representative of HF*r*EF, and may be eligible for consideration of treatment with bisoprolol, carvedilol, or metoprolol succinate, as per clinical practice guideline recommendations for HF*r*EF.
- The following dose equivalents have been developed to assist practitioners who elect to convert their patients to a beta-blocker with established mortality benefit in HF*r*EF; and may be used for site level evaluation, education and intervention, as indicated.

Note: Recommendations are not based on head-to-head comparison trials; dosage conversions are derived from the initial, mean, and target doses reported in long-term, randomized, placebo-controlled outcome trials and from national clinical practice guideline recommendations. The following may be modified based on clinical judgment and may be used if conversion deemed appropriate.

Atenolol	Metoprolol IR[a]	Bisoprolol	Carvedilol[b]	Metoprolol XL[a]
25 mg once or divided twice daily	6.25 to 12.5 mg twice daily	1.25 mg once daily	3.125 mg twice daily	25 mg once daily (12.5 mg once daily if > NYHA class II)
50 mg once or divided twice daily	12.5 to 25 mg twice daily	2.5 mg once daily	6.25 mg twice daily	50 mg (or 25 mg) once daily
75 mg once or divided twice daily	25 to 50 mg twice daily	5 mg once daily	12.5 mg twice daily	100 mg (or 50 mg) once daily
100 mg once or divided twice daily	50 to 100 mg twice daily	10 mg once daily	25 mg twice daily (may titrate to 50 mg twice daily if ≥ 85 kg)	200 mg (or 100 mg titrated to 200 mg) once daily

[a] Metoprolol IR=immediate release metoprolol tartrate; Metoprolol XL=sustained release metoprolol succinate
[b] Dosing recommendations for carvedilol; carvedilol CR (extended-release formulation dosed once daily) also available non-formulary

For additional discussion, information on recommended target doses, and references: refer to Beta-Blockers in Heart Failure, Clinical Recommendations (Rev Dec 2016) . ■