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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

GENVOYA (elvitegravir, cobicistat, emtricitabine, and tenofovir alafenamide) and STRIBILD (elvitegravir, cobicistat, emtricitabine, and tenofovir disoproxil fumarate): DO NOT ABBREVIATE DRUG NAMES

The Institute for Safe Medication Practices (ISMP) has received 2 reports of medication errors resulting from the way provider order entry systems display **GENVOYA** (elvitegravir, cobicistat, emtricitabine, and tenofovir *alafenamide*) and **STRIBILD** (elvitegravir, cobicistat, emtricitabine, and tenofovir *disoproxil fumarate*). In one error, the computer system presented the medication using abbreviated generic drug names only (i.e., "Elviteg-Cobic-Emtricit-TenofAF"). Upon hospital admission of a patient previously taking **GENVOYA** (elvitegravir, cobicistat, emtricitabine, and tenofovir *alafenamide*), the pharmacy mistakenly dispensed **STRIBILD** (elvitegravir, cobicistat, emtricitabine, and tenofovir *disoproxil fumarate*) instead due to the shortened form of the names in the electronic system. Although the patient received one dose of the wrong medication, no harm occurred.

Aside from the likeness in generic name, potential confusion between **GENVOYA** (elvitegravir, cobicistat, emtricitabine, and tenofovir *alafenamide*) and **STRIBILD** (elvitegravir, cobicistat, emtricitabine, and tenofovir *disoproxil fumarate*) can result from the following additional *similarities*:

- Both are manufactured by Gilead;
- Both are fixed-dose combinations of 4 agents in one tablet for oral administration :
  - Each **GENVOYA** tablet contains 150 mg of elvitegravir, 150 mg of

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NEWSWORTHY...

from the pbm

- Topical Skin Products Recall Due to Microbial Contamination – 08/29/2016 - National PBM Patient Level Recall Communication
- Liquid Products Recall (PharmaTech) Due to Potential Risk of Product Contamination – 08/12/2016 - National PBM Patient Level Recall Communication
- Amikacin Recall Due to Particulate Matter in Vials - 08/08/2016 - National PBM Patient Level Recall Communication
- Bactroban (Mupirocin) Recall Expansion – 08/04/2016 - National PBM Patient Level Recall Communication

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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.

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NEWSWORTHY...

from the fda

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PAIN MANAGEMENT

FDA warns about serious risks and death when combining opioid pain or cough medicines with benzodiazepines; requires its strongest warning

8/31/2016

FDA will add *Boxed Warnings* to the drug labeling of prescription opioid pain as well as prescription opioid cough medicines, along with benzodiazepines due to findings from FDA reviews in addition to data from published studies that show:

- increasing trend in concomitant dispensing of opioid analgesics and benzodiazepines;
- increasing frequency of combined benzodiazepine and prescription opioid misuse, abuse, and overdose, as measured by national emergency department (ED) visit and overdose death rates (from prescribed or greater than prescribed doses);
- increased risk of adverse events occurring in patients dispensed both opioid analgesics and benzodiazepines.

In an effort to decrease the combined use of opioids and benzodiazepines, or of opioids and other CNS depressants together, FDA recommends that health care professionals:

- *Reserve concomitant prescribing of opioid analgesics with benzodiazepines or other CNS depressants for use in patients for whom alternative treatment options are inadequate.*
- *Avoid use of prescription opioid cough medications in patients taking benzodiazepines or other CNS depressants.*
- *If these medicines are prescribed together:*
  - ⇒ *prescribe a lower initial dose than indicated of the opioid, benzodiazepine, and/or other CNS depresssant being initiated;*
  - ⇒ *titrate based on clinical response;*
  - ⇒ *limit the dosages and duration of the opioid, benzodiazepine, and/or other CNS depressant to the minimum possible while achieving the desired clinical effect.*
- *Monitor patients closely for respiratory depression and sedation.*
- *Warn patients and caregivers about the risks of sedation, respiratory depression, coma, and/or death if opioids are used with benzodiazepines, alcohol, or other CNS depressants (including illicit or recreational drugs).*
- *Advise patients not to drive or operate heavy machinery until the effects of concomitant use of the opioid and benzodiazepine or other CNS depressant have been determined.*
- *Screen patients for risk of substance-use disorders, including opioid abuse and misuse, and warn them of the risk for overdose and death associated with the use of additional CNS depressants, including alcohol and illicit or recreational drugs.*

Helping to achieve safe medication use

GENVOYA (elvitegravir, cobicistat, emtricitabine, and tenofovir alafenamide) and STRIBILD (elvitegravir, cobicistat, emtricitabine, and tenofovir disoproxil fumarate): DO NOT ABBREVIATE DRUG NAMES

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cobicistat, 200 mg of emtricitabine, and 10 mg of tenofovir alafenamide (TAF) (equivalent to 11.2 mg of tenofovir alafenamide fumarate).

- Each **STRIBILD** tablet contains 150 mg of elvitegravir, 150 mg of cobicistat, 200 mg of emtricitabine, and 300 mg of tenofovir DF (equivalent to 245 mg of tenofovir disoproxil).
- Both dosage forms resemble each other:
  - **GENVOYA** tablets are green, capsule-shaped, film-coated tablets, debossed with "GSI" on one side of the tablet and the number "510" on the other side of the tablet.
  - **STRIBILD** tablets are green, capsule shaped, film -

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Helping to achieve safe medication use

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coated, and debossed with "GSI" on one side and the number "1" surrounded by a square box (1) on the other side.

- Both have once a day administration;
- Both treat human immunodeficiency virus-type 1 (HIV-1) infection.

However, these products are not interchangeable due to their differences in tenofovir salt formulation. **STRIBILD** (elvitegravir, cobicistat, emtricitabine, and tenofovir *disoproxil fumarate*) contains tenofovir *disoproxil fumarate,* a prodrug whose high circulating plasma levels of the active metabolite tenofovir diphosphate have been associated with increases in risk of renal and bone toxicity. In comparison, **GENVOYA** (elvitegravir, cobicistat, emtricitabine, and tenofovir *alafenamide*) contains tenofovir *alafenamide,* a prodrug that delivers four times greater intracellular concentrations of the active metabolite tenofovir diphosphate, allowing for a much lower dose of tenofovir *alafenamide.* Due to tenofovir *alafenamide*'s reduced dose, plasma exposure is diminished by 90% compared to tenofovir *disoproxil fumarate* leading to decreased risk of renal and bone toxicity.

Within the past year, the FDA has approved three fixed-dose combination products containing tenofovir *alafenamide.* Among the tenofovir-containing fixed combination products listed on the VA National Formulary (http://www.pbm.va.gov/PBM/NationalFormulary.asp), tenofovir *disoproxil fumarate* preparations as well as tenofovir *alafenamide* formulations are available (Table 1, page 4). Distinction between agents containing tenofovir *disoproxil fumarate* versus tenofovir *alafenamide* when ordering medications using computerized provider order-entry systems will help providers to select appropriate therapy taking into consideration patient comorbidities and risk factors as recommended by national guidelines while avoiding adverse outcomes. For more guidance on antiretroviral regimen selection and place in therapy, visit: DHHS HIV Guidelines.

In order to prevent future mix-ups during the medication ordering process while using electronic ordering systems, ISMP recommends:

- Displaying both the brand and generic names of the drug when possible;
- Not abbreviating the drug names.

Within the VA, pharmacy can take the following steps inside the computerized drug-order entry system to reduce potential look-alike error with the agents specified by ISMP as well as other combination products comprised of different salt formulations of tenofovir that may not have been associated with a reported error but bear the same risk:

- Add a short descriptor (less than 74 characters) to "Display Restriction/Guidelines". For example: *(NOTE: GENVOYA product contains tenofovir ALAFENAMIDE) and (NOTE: STRIBILD product contains tenofovir DISOPROXIL FUMARATE)*. As blue line text, this descriptor displays as dialog and does not become part of order.
- Add brand name as a synonym so that it appears in addition to the full generic drug name with salt in VistA pharmacy orderable item file #50.7. For example:
  - *GENVOYA <COBICISTAT/ELVITEGRAVIR/EMTRIC/ TENOF ALAFENAMIDE TAB, ORAL>*
  - *STRIBILD <COBICISTAT/ELVITEGRAVIR/EMTRIC/ TENOF DISOPR FUMARATE TAB, ORAL>*
  - *ODEFSEY <EMTRIC/RILPIVIRINE/TENOF ALAFENAMIDE TAB, ORAL>*
  - *COMPLERA <EMTRIC/RILPIVIRINE/TENOF DISOPR FUMARATE TAB, ORAL>*
  - *DESCOVY<EMTRIC/ TENOF ALAFENAMIDE TAB, ORAL>*
  - *TRUVADA <EMTRIC/ TENOF DISOPR FUMARATE TAB, ORAL>*

Moreover, with respect to the drug product pair highlighted by ISMP, pharmacy should review their stock for **GENVOYA** (elvitegravir, cobicistat, emtricitabine, and tenofovir *alafenamide*) and **STRIBILD** (elvitegravir, cobicistat, emtricitabine, and tenofovir *disoproxil fumarate*), and ensure that a method is in place to distinguish between the two agents in order to avoid any potential look-alike confusion (i.e., warning stickers/labels, separate product placement on shelves).

REFERENCES:

1. Institute for Safe Medication Practices (ISMP). Dnt abbr drg nms. *ISMP Medication Safety Alert! Acute Care* August 2016; 21 (17): 4.
2. **GENVOYA®** (elvitegravir, cobicistat, emtricitabine, and tenofovir *alafenamide*) product package insert. Foster City, CA: Gilead Sciences, Inc; September 2016.
3. **STRIBILD®** (elvitegravir, cobicistat, emtricitabine, and tenofovir *disoproxil fumarate*) product package insert. Foster City, CA: Gilead Sciences, Inc; February 2016.
4. **ODEFSEY®** (emtricitabine, rilpivirine, and tenofovir alafenamide) product package insert. Foster City, CA: Gilead Sciences, Inc; March 2016.
5. **COMPLERA®** (emtricitabine, rilpivirine, tenofovir disoproxil fumarate) product package insert. Foster City, CA: Gilead Sciences, Inc; February 2016.
6. **DESCOVY®** (emtricitabine and tenofovir alafenamide) product package insert. Foster City, CA: Gilead Sciences, Inc; April 2016.
7. **TRUVADA®** (emtricitabine/tenofovir disoproxil fumarate) product package insert. Foster City, CA: Gilead Sciences, Inc; April 2016.

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Helping to achieve safe medication use

GENVOYA (elvitegravir, cobicistat, emtricitabine, and tenofovir alafenamide) and STRIBILD (elvitegravir, cobicistat, emtricitabine, and tenofovir disoproxil fumarate): DO NOT ABBREVIATE DRUG NAMES

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Table 1. Tenofovir-containing fixed-dose combination products available as either tenofovir *disoproxil fumarate* or tenofovir *alafenamide* on the VA National Formulary.

NAME	APPROVAL	INDICATION	DOSAGE FORM & STRENGTH	RECOMMENDED ADULT DOSE	VA NATIONAL FORMULARY STATUS
GENVOYA® (elvitegravir, cobicistat, emtricitabine, and tenofovir *alafenamide*)	2015	Treatment of HIV-1 infection (complete regimen)	Four-drug fixed dose combination product containing 150 mg of elvitegravir, 150 mg of cobicistat, 200 mg of emtricitabine, and 10 mg of tenofovir alafenamide (TAF) (equivalent to 11.2 mg of tenofovir alafenamide fumarate). The tablets are green, capsule-shaped, film-coated tablets, debossed with "GSI" on one side of the tablet and the number "510" on the other side of the tablet.	One tablet taken orally once daily with food	Yes
STRIBILD® (elvitegravir, cobicistat, emtricitabine, and tenofovir *disoproxil fumarate*)	2012	Treatment of HIV-1 infection (complete regimen)	Four-drug fixed dose combination product containing 150 mg of elvitegravir, 150 mg of cobicistat, 200 mg of emtricitabine, and 300 mg of tenofovir DF (equivalent to 245 mg of tenofovir disoproxil). The tablets are green, capsule shaped, film coated, and debossed with "GSI" on one side and the number "1" surrounded by a square box (1) on the other side.	One tablet taken orally once daily with food	Yes
ODEFSEY® (emtricitabine, rilpivirine, and tenofovir alafenamide)	2016	Treatment of HIV-1 infection (complete regimen)	Three-drug fixed dose combination product containing 200 mg of emtricitabine (FTC), 25 mg of rilpivirine (RPV) (equivalent to 27.5 mg of rilpivirine hydrochloride), and 25 mg of tenofovir alafenamide (TAF) (equivalent to 28 mg of tenofovir alafenamide fumarate). The tablets are gray, capsule-shaped, film-coated and debossed with "GSI" on one side and "255" on the other side.	One tablet taken orally once daily with a meal	Yes
COMPLERA® (emtricitabine, rilpivirine, tenofovir disoproxil fumarate)	2011	Treatment of HIV-1 infection (complete regimen)	Three-drug fixed dose combination product containing 200 mg of emtricitabine (FTC), 27.5 mg of rilpivirine hydrochloride (equivalent to 25 mg of rilpivirine), and 300 mg of tenofovir disoproxil fumarate (tenofovir DF or TDF, equivalent to 245 mg of tenofovir disoproxil). The tablets are purplish pink, capsule shaped, film coated, debossed with "GSI" on one side, and plain faced on the other side.	One tablet taken orally once daily with food	Yes
DESCOVY® (emtricitabine and tenofovir alafenamide)	2015	Treatment of HIV-1 infection (in combination with other antiretroviral agents)	Two-drug fixed dose combination product containing 200 mg of emtricitabine (FTC) and 25 mg of tenofovir alafenamide (TAF) (equivalent to 28 mg of tenofovir alafenamide fumarate). The tablets are blue, rectangular-shaped, film-coated, debossed with "GSI" on one side and "225" on the other side.	One tablet taken orally once daily with or without food	Yes
TRUVADA® (emtricitabine/ tenofovir disoproxil fumarate)	2004	Treatment of HIV-1 infection (in combination with other antiretroviral agents); Pre-exposure prophylaxis	*For ADULT patients with body weight greater than or equal to 35 kg:* Two-drug fixed dose combination product containing 200 mg of emtricitabine and 300 mg of tenofovir disoproxil fumarate (equivalent to 245 mg of tenofovir disoproxil). The tablets are blue, capsule-shaped, film-coated, debossed with "GILEAD" on one side and with "701" on the other side. Also available in three additional dosage strengths for PEDIATRIC patients weighing 17 kg to less than 35 kg and are therefore not included in this list.	*Treatment of HIV 1 infection (in combination with other antiretroviral agents)* - One tablet (containing 200 mg of emtricitabine and 300 mg of tenofovir disoproxil fumarate) once daily taken orally with or without food; *Pre-exposure prophylaxis* - One tablet (containing 200 mg of emtricitabine and 300 mg of tenofovir disoproxil fumarate) once daily taken orally with or without food.	Yes

Getting the most from our safety surveillance

OPIOID SAFETY IN THE VA

Over the last four years, VA has focused on opioid safety with efforts to provide appropriate pain care utilizing standardized evidence-based prescribing practices that safeguard against harm and abuse. One such area of potential harm highlighted by the FDA in a recent Drug Safety Communication concerns the combined use of opioid-containing products with benzodiazepines. FDA recently reviewed evidence suggesting a 41% increase in concomitant prescribing of opioids with benzodiazepines and a risk of harm (i.e., emergency department visits and overdose deaths) with co-use of these agents, which prompted their new requirement of adding Boxed Warnings to the drug labeling of these products (see page 2). Within the VA, various clinical resources and programs help to address the many challenges of pain management with opioids, such as VA's Opioid Safety Initiative (OSI), which measures and monitors opioid utilization trends and prescribing patterns nationally within the VA system-wide.

Aimed at reducing high-risk opioid prescribing, VA chartered the OSI in 2012, and finished expanding the program nationwide approximately 1 year later. The OSI is a VA-wide interdisciplinary program whose intent is not to dictate which patients should receive opioid therapy. Rather, the goal of the initiative is to:

- identify Veterans at immediate, short term, and long term risk of harm associated with high-dose opioid therapy and to develop an individualized clinical action plan to mitigate risks;
- offer provider education and training to enhance competencies and to promote compliance to clinical practice guidelines for opioid therapy in the management of chronic pain; and
- encourage utilization of existing tools and resources to promote organizational/system improvements to support providers in the delivery of safe and effective opioid therapy in the context of integrated, team-based pain management.

The OSI assesses national trends in opioid consumption and prescribing practices within the VA system-wide using a data warehouse approach to measure key clinical elements such as the number of VA pharmacy users dispensed an opioid prescription, opioid quantity, average morphine equivalent daily doses (MEDD) prescribed, the number of VA pharmacy users on long-term opioids who receive a urine drug screen, and concomitant use of opioid and benzodiazepine derivative, sedative/hypnotic therapies.

VA's OSI addresses clinically inappropriate prescribing of opioids such as concomitant use of opioid and benzodiazepine derivative, sedative/hypnotic therapies because the combination imparts a higher risk of adverse events. Interestingly, OSI metrics show 57,734 fewer patients receiving opioids and benzodiazepines together (from 122,633 patients in the last quarter of fiscal year [FY] 2012 to 64,899 patients in the third quarter of FY 2016). This translates to a 47 percent reduction nationally within the VA system-wide (Figure 1), in contrast to the upward trend indicated by the FDA.

This decrease has occurred as a result of the synergistic activities of interdisciplinary collaborative programs within the VA which jointly work to further enhance and guide appropriate use of opioids. Some of these initiatives include:

- Opioid Therapy Risk Report (OTRR), a tool that allows VA providers to review patient-specific clinical information about the dosages of narcotics and other sedative medications; comorbid conditions and potential risk factors; and monitoring data to aid in the review as well as management of complex patients.
- VISN dashboards, which facilitate VA providers with a review of all pertinent clinical data related to pain treatment in one place for a more efficient level of management.
- Academic Detailing, where specialty teams visit facilities and provide on-site education and training to health professionals and teams.
- Office of Mental Health Operations (OMHO) – Psychotropic Drug Safety Initiative (PDSI), which addresses appropriate opioid management in mental health patients receiving treatment with psychiatric medications.
- Complementary and integrative medicine to enhance management of chronic pain symptoms utilizing various forms of treatments including acupressure, acupuncture, biofeedback, chiropractic services, exercise, heated pool therapy, hypnosis/hypnotherapy, massage therapy, meditation, occupational therapy, physical therapy, recreational therapy, relaxation, tai chi, transcutaneous electrical nerve stimulation, yoga and other services.

Although we see a remarkable improvement in combined use, VA will continue to expand on its opioid initiatives and augment its mechanisms to monitor and promote the appropriate use of opioids to ensure the safety of our Veteran patients.

REFERENCES:

1. FDA Drug Safety Communication: FDA warns about serious risks and death when combining opioid pain or cough medicines with benzodiazepines; requires its strongest warning. http://www.fda.gov/Drugs/DrugSafety/ucm518473.htm . (Accessed August 31, 2016).
2. Internal data. ■

Figure 1. Unique Patients Dispensed Opioid (including Tramadol) and Benzodiazepine Therapies Over Time. Trends in concomitant use within the VA show a decrease over the past four years.