

MEDICATION

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

SAFETY IN SECONDS

Helping to achieve safe medication use

ENOXAPARIN LOOK-ALIKE CONFUSION REPORTED BY ISMP

The Institute for Safe Medication Practices (ISMP) received reports of mix-ups between enoxaparin prefilled syringes and other drugs in similar-looking syringes. In one instance, Relistor (methylnaltrexone) injection 12mg/0.6mL from Salix Pharmaceuticals (indicated for opioid-induced constipation) was mistaken for generic enoxaparin 150mg/mL prefilled syringes manufactured by Amphastar Pharmaceuticals (Figure 1). In another case, look-alike product confusion occurred between fondaparinux 2.5mg/0.5mL from Dr. Reddy's Laboratories and 30mg/0.3mL syringes of enoxaparin from Teva (Figure 2). In each occurrence, similarly colored syringe plunger and clear plastic casing contributed to the look-alike error. Fortunately, no wrong product reached the patient. As a result of the errors, however, ISMP recommends that these products should remain in their cartons or blister packs until the time of administration to maintain distinguishability.

REFERENCES:

Institute for Safe Medication Practices. Safety Briefs: Fooled by enoxaparin look-alikes. *ISMP Medication Safety Alert! Acute Care*. 20(16): 1-2. August 13, 2015



Figure 1. Relistor (top) and enoxaparin (bottom) syringes are almost identical in size and color.



Figure 2. Casing and plunger similarities between fondaparinux (bottom) and enoxaparin (top) contribute to look-alike confusion.

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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

- BD Syringes and Loss of Drug Potency – 08-31-2015 - [National PBM Bulletin](#)

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from the fda

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ENDOCRINOLOGY

[FDA warns that DPP-4 inhibitors for type 2 diabetes may cause severe joint pain](#)

8/28/2015

Severe and disabling joint pain with the use of dipeptidyl peptidase-4 (DPP-4) inhibitors has been reported in the FDA Adverse Event Reporting System (FAERS) database (33 cases from October 2006 to December 2013) and the medical literature (7 case reports, 2 of which appeared in the FAERS database).

Out of the 33 cases identified in FAERS:

- Each involved the use of one or more DPP-4 inhibitors: sitagliptin (n=28), saxagliptin (n=5), linagliptin (n=2), alogliptin (n=1), and vildagliptin (n=2; not marketed in the United States).
- All 33 patients experienced arthralgia that resulted in a substantial reduction in their prior level of activity.
 - 10 patients were hospitalized due to disabling joint pain.
 - 21 patients were treated for arthritis with drug therapies that included corticosteroids, nonsteroidal anti-inflammatory drugs, methotrexate, and immune-modulating drugs.
- The time to onset of symptoms following initiation of drug therapy varied from 1 day to years.
 - 22 cases reported symptoms within 1 month of initiation of treatment with a DPP-4 inhibitor.
 - In 20 cases, the DPP-4 inhibitor was suspected as a possible cause of arthralgia and was discontinued within a month following the onset of symptoms. However, 8 of the remaining 13 cases reported a period of 44 days to 1 year between the onset of symptoms and discontinuation of the DPP-4 inhibitor.
- Patients experienced relief of symptoms upon discontinuation of the medication.
 - In 23 of the 33 cases, symptoms resolved less than 1 month after discontinuation of the drug.
- Some patients had a recurrence of severe joint pain when restarted on either their original DPP-4 inhibitor medication or another DPP-4 inhibitor.
 - 8 of the 33 cases documented a positive rechallenge.

Out of the 7 cases identified in the medical literature:

- All developed arthralgia after starting therapy with either sitagliptin (n=6) or vildagliptin (n=1);
- 6 patients had partial or complete resolution of symptoms within 6 weeks of discontinuing the drug;
- 1 case reported the pain to be disabling; and
- None reported the need for hospitalization.

FDA recommends that health care professionals should:

- Instruct patients to not stop taking their DPP-4 inhibitor medicine, and to contact their health care professional right away if they experience severe and persistent joint pain.
- Consider DPP-4 inhibitors as a possible cause of severe joint pain and discontinue the drug if appropriate.

DERMATOLOGY

[FDA warns of severe adverse events with application of Picato \(ingenol mebutate\) gel for skin condition; requires label changes](#)

8/21/2015

FDA has received adverse event reports consisting of severe eye injuries (severe eye pain, chemical conjunctivitis, corneal burn, eyelid edema, eyelid ptosis, periorbital edema); severe allergic reactions (including anaphylaxis, generalized rashes, and allergic contact dermatitis); as well as herpes zoster reactivation associated with the use of ingenol mebutate (Picato gel) for the treatment of actinic keratosis. These adverse events resulted from inappropriate application of the topical in a manner not consistent with the recommendations in the label, which involved wrong application site size and location, wrong strength for treatment area, wrong treatment duration, wrong technique, wrong storage conditions, and accidental exposure. FDA requires changes to the label to warn about these new safety risks and to provide additional directions on the safe and appropriate application of the

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product. FDA recommends that health care professionals should educate patients on appropriate use according to instructions in the product label, such as:

- Picato gel should only be applied on one skin area at a time only to skin lesions diagnosed as actinic keratosis. The application area should be no larger than approximately 2 inches by 2 inches (25 cm²), which is about the size of a child's palm.
- Avoid applying Picato gel in, near, and around the eyes, in the mouth, and on the lips.
- If Picato gel gets into your eyes, immediately flush them with large amounts of water and get medical care right away.
- To avoid accidental transfer of Picato gel to the eyes or other areas, or to another person:
 - Wash your hands well with soap and water after applying Picato gel.
 - Allow the treated area to dry for 15 minutes after application.
 - Avoid showering, washing, and touching the treated area, or participating in activities that cause excessive sweating, for 6 hours after treatment. However, after 6 hours, you may wash the area with a mild soap.
 - Keep out of the reach of children.
- Do NOT:
 - Mix Picato gel with other topical medications or lotions.
 - Apply make-up or insert contact lenses right after applying Picato gel.
 - Apply Picato gel less than 2 hours before going to bed.
- Store Picato gel in a refrigerator. Do not freeze the product.

Getting the most from our safety surveillance

WARFARIN PRODUCT CONFUSION

Earlier this year, a National Contract introduced a new warfarin product manufactured by Exelan/Invagen to the VA Health Care System. However, in the past months since the contract was announced, medical centers have experienced incidents where patients presented with elevated international normalized ratios (INRs) ensuing from extra warfarin dosing without any documented bleeding. In these cases, the tablet confusion occurred at the patient level, where patients have taken the wrong tablet in their home environment. One facility described that 2 patients with supratherapeutic INRs self-reported that they had “double-dosed” on warfarin. They took their warfarin tablet and what they thought was one of their other medications but was in reality also a warfarin tablet again since the new warfarin tablets now bear a similar appearance to one of their other routine medications due to the round shape and color. As an example (but not specific to the aforementioned cases), hydrochlorothiazide 25mg (manufactured by Teva) and warfarin 5mg (manufactured by Exelan) share similarities in dosage form, shape, size, and color (Figures 1 and 2). At another site, a patient with usual therapeutic INR presented with a point-of care INR > 8, followed by a venous INR > 11. The patient's son had verified that when looking at the patient's medications at home, the patient had been taking both the round (Exelan) 2.5mg tablets and the

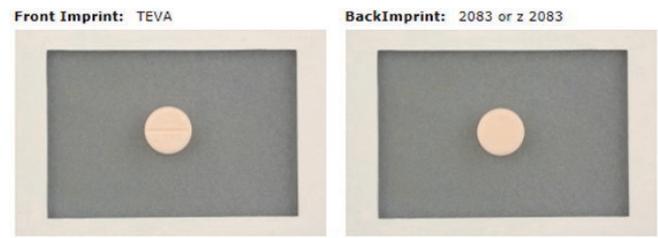


Figure 1. Hydrochlorothiazide 25mg manufactured by Teva resembles the warfarin tablet manufactured by Exelan in Figure 2 in color, shape, and size.



Figure 2. Similar appearance of this warfarin tablet from Exelan to the hydrochlorothiazide tablet pictured in Figure 1 can contribute to look-alike product confusion.

Getting the most from our safety surveillance

WARFARIN PRODUCT CONFUSION

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oblong (Golden State) 2.5mg tablets every day not realizing that both were warfarin.

At the time of the change in contract, PBM notified the field, including direct communication with anticoagulation pharmacists, along with providing a customizable patient letter template to use to inform patients of the change in warfarin manufacturer and product. Despite these efforts, concerns with product confusion continue to emerge. As such, PBM/MedSAFE recommends that:

For all patients newly switching over to the Exelan product, pharmacists should:

- Affix auxiliary labels and stickers to patients' prescription bottles of affected product that warn of a new manufacturer and new appearance in medication.
- Counsel patients prescribed affected product at the point-of-care, specifically regarding the use of a new warfarin manufacturer and differences in medication appearance with use of the new warfarin product.
- A sample letter can be found at the following internal link: <https://vaww.cmopnational.va.gov/cmop/PBM/Clinical%20Guidance/Therapeutic%20Interchange%20Guidance/Warfarin%20Generic%20Switch%20Patient%20Letter%202015.doc> .

This template can be altered according to site-specific needs. In addition, patient letters can be customized and notify the

patient of the change in manufacturer, size, shape, color as well as include colored pictures of the new tablets in order to help minimize confusion with the transition.

For patients who have an INR change that is readily not understood, anticoagulation staff should:

- Verify new product awareness and appropriate use with the patient.

Providers should continue to report any adverse reactions with the use of warfarin by entering the information into CPRS' Allergies/ Adverse Reactions field and/or via local reporting mechanisms.

Providers should also report these incidents to VA ADERS. Reporters can enter the elevated INR and also the free text symptoms of "product substitution issue" as well as "medication error". The manufacturer and lot number should be included in tab 8 of the report as well.

In addition, adverse events should be reported, as appropriate, to the VA ADERS program and FDA MedWatch (1-800-FDA-1088, fax 1-800-FDA-0178, online at <https://www.accessdata.fda.gov/scripts/medwatch/medwatch-online.htm> , or by mail). ■

REFERENCES:

Internal Data.