

MEDICATION

A MONTHLY PUBLICATION FROM VA MEDSAFE:
VA'S COMPREHENSIVE PHARMACOVIGILANCE CENTER**SAFETY IN SECONDS**

Helping to achieve safe medication use

TWO – COMPONENT VACCINES: ERRORS AND PREVENTION

A recent analysis from the U.S. Food and Drug Administration (FDA) and the Centers for Disease Control and Prevention (CDC) showed errors associated with the 2-component vaccine Menveo (meningococcal groups A/C/Y, W-135 diphtheria conjugate vaccine) which comes as a lyophilized (powdered) portion and a liquid constituent co-packaged in separate vials that require mixing prior to administration. Menveo is a conjugate vaccine that prevents invasive meningococcal disease caused by *Neisseria meningitidis* serogroups A, C, Y, and W-135. Failure to prepare this vaccine as directed by the manufacturer can lead to lack of protection against the aforementioned pathogens. Individuals may not realize their vulnerability to a disease if an error goes unrecognized or unreported. Reported errors include:

- Administration of the liquid component

alone without the lyophilized component (66%);

- Administration of the lyophilized component, reconstituted with sterile water, saline, a different liquid vaccine, or an unspecified diluent (34%).

In the case of administration of an improperly prepared dose of Menveo, providers can administer a repeat dose prepared according to the manufacturer's instructions at any time.

Similar errors have been reported with other 2-component vaccines packaged as separate liquid and lyophilized parts that must be combined before administration, such as Pentacel (diphtheria and tetanus toxoids, acellular pertussis, poliovirus, *Haemophilus b* conjugate) as well as vaccines with diluents. Vaccines requiring reconstitution

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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

- Idelalisib Safety – 03/29/2016 - [National PBM Bulletin](#)

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from the fda

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PAIN MANAGEMENT

[FDA warns about several safety issues with opioid pain medicines; requires label changes](#)

3/22/2016

FDA warns about several safety issues associated with the opioid class of medications used to manage pain. FDA requires label changes to convey these risks, which include serotonin syndrome, adrenal insufficiency, and androgen deficiency.

Serotonin syndrome

- FDA's Adverse Event Reporting System (FAERS) shows 43 cases of serotonin syndrome associated with concomitant use of opioids and other serotonergic drugs from January 1, 1969 to June 12, 2013.
- Onset of symptoms typically occurs within several hours to a few days of concomitant use but may occur later (i.e., after dose increase).
- Serotonin syndrome may take place within recommended dosage ranges.
- Symptoms may include mental status changes (e.g., agitation, hallucinations, coma); autonomic instability (e.g., tachycardia, labile blood pressure, or hyperthermia); or neurologic abnormalities (e.g., hyperreflexia, incoordination, or rigidity).
- **Healthcare professionals should:**
 - Determine whether patients are taking serotonergic drugs concomitantly with opioid medications.
 - Discontinue opioid treatment and/or use of the concomitant serotonergic drug if serotonin syndrome is suspected.
 - Educate patients on the symptoms of serotonin syndrome and advise them to seek medical attention immediately if symptoms develop.

Adrenal insufficiency

- 37 cases of adrenal insufficiency from January 1, 1969 to February 5, 2014 in the FAERS database were identified in patients taking opioids.
- Information collected from cases does not suggest whether one particular opioid has a greater association than another.
- Symptoms are nonspecific and may include: nausea, vomiting, anorexia, fatigue, weakness, dizziness, and hypotension.
- Symptom onset in reported cases occurred within one day of initiation of opioid therapy to more than a year.
- **Healthcare professionals should:**
 - Confirm with diagnostic testing if adrenal insufficiency is suspected.
 - If diagnosis is confirmed, treat patient with physiologic replacement doses of corticosteroids and wean off of opioid to allow adrenal function to recover.
 - If the opioid can be discontinued, perform additional assessment of adrenal function to determine whether treatment of corticosteroids can be discontinued.

Androgen deficiency

- Studies demonstrated decreased gonadal hormones in men and women taking long-term opioids.
- Symptoms include low libido, impotence, erectile dysfunction, amenorrhea, or infertility.
- Limitations in research design prevent a definitive association of androgen deficiency with long-term opioid use or whether symptoms can be attributed to other factors such as the patient's underlying medical condition warranting opioid treatment; physical, mental, or life stressors; weight changes; or concomitant medication or supplement use.
- **Healthcare professionals should:**
 - Perform laboratory evaluation on patients presenting with symptoms or signs of androgen deficiency.

Getting the most from our safety surveillance

UPDATE: INTRALIPID I.V. FAT EMULSION PRODUCTS IN BIOFINE CONTAINERS—PARTICULATE MATTER OBSERVED

Our [Issue 1; Volume 6; January 2016](#) publication addressed a safety alert from Baxter regarding particulate matter observed in Intralipid I.V. Fat Emulsion 20% products in Biofine containers as well as recommended safety measures to prevent harm. Baxter recently released an update to their original warning which identifies that the **Baxter Automated Compounding Device Non-vented Inlet REF 173 (SKU: H938173)** and **Vented Spikes on the PINNACLE Compounder Sets (SKU: 2112342/2112341/2112343/2112344)** associated with Baxter's EXACTAMIX and B. Braun's PINNACLE automated compounding devices are at greater risk of generating particles when spiked using incorrect technique. The notice maintains that no adverse events have been reported with this issue. Affected products include those listed in Table 1. There is one difference in the below list compared to the previously mentioned products: Intralipid, 20% 250 milliliter [ML] (product code 2B6062, all lot numbers) now has a new NDC number of 0338-0519-09 (instead of 0338-0519-12 as previously reported).

Precautionary recommendations remain the same as follows:

- *Refrain from using Intralipid in Biofine containers with automated compounding sets. Manual compounding and direct infusion sets can be continued.*
- *Examine the product carefully for particulate matter in a well-lit environment before infusing into a patient.*
- *Do not use the product if particulate matter is present.*
- *Use a 1.2 micron filter with Intralipid and admixtures containing Intralipid. Filters of less than 1.2 micron pore size must not be used.*
- *Follow the instructions for spiking as provided below:*
 - *Place the bag on a clean and flat surface;*
 - *Hold the base of the infusion port and insert the spike through the center of the septum by rotating the wrist slightly;*
 - *Assure that the spike is inserted straight into the port without an angle.*

Table 1. Affected Products.

PRODUCT CODE	DESCRIPTION	NDC	LOT NUMBER
2B6065	INTRALIPID®, 30% 500 ML	0338-0520-13	All Lot Numbers
2B6064	INTRALIPID®, 20% 1000 ML	0338-0519-14	All Lot Numbers
2B6063	INTRALIPID®, 20% 500 ML	0338-0519-13	All Lot Numbers
2B6062	INTRALIPID®, 20% 250 ML	0338-0519-09	All Lot Numbers
2B6061	INTRALIPID®, 20% 100 ML	0338-0519-58	All Lot Numbers

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TWO-COMPONENT VACCINES: ERRORS AND PREVENTION

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should only be combined with the respective diluent or counter-part supplied by the manufacturer for that vaccine. The Institute for Safe Medication Practices (ISMP) recommends that FDA improve vaccine labeling and packaging requirements to reduce the risk of errors with 2-component vaccines. ISMP also recommends that healthcare practitioners:

- Clearly label or distinguish each component of the vaccine;
- Store 2-component vaccines together if storage requirements do not differ and label to remind staff to use both vials;
- Employ technology such as barcode scanning prior to mixing and administration;
- Maintain a vaccination record or log before administration

to confirm appropriate selection or preparation of both components of 2-component vaccines;

- Educate staff on the differences between 2-component vaccines and vaccines packaged with specific diluents.

REFERENCES:

1. Su JR, Miller ER, Duffy J, Baer BM, Cano MV. *Notes from the Field: Administration Error Involving a Meningococcal Conjugate Vaccine* — United States, March 1, 2010–September 22, 2015. *MMWR Morb Mortal Wkly Rep* 2016;65:place_holder_for_early_release:161–162. DOI: <http://dx.doi.org/10.15585/mmwr.mm6506a4>
2. Institute for Safe Medication Practices (ISMP). Government and industry fail to protect the public when they suggest “carefully following instructions” is enough to prevent vaccine errors. *ISMP Medication Safety Alert! Acute Care* February 25 2016; 21 (4): 1-4. ■