

MEDICATION SAFETY IN SECONDS

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

Helping to achieve safe medication use

CONTINUING RISKS WITH FENTANYL PATCHES

According to the Institute for Safe Medication Practices' (ISMP) latest Quarterly Report, safety issues persist with opioid analgesics, particularly with fentanyl (Duragesic) patches. Out of a total of 1890 reports of serious injury related to fentanyl (Duragesic) patches in 2012, approximately 60% (n=1148) ensued from a medication error while around 40% (n=808) involved a product problem (i.e., manufacturing defect). Examples of medication errors identified from the aforementioned reports include:

- Prescribing errors (48 cases)
- Patient self-administration errors
 - Omitting a dose (130 cases)
 - Putting a patch on an inappropriate site (115 cases)
 - Leaving the patch on too long (40 cases)
 - Accidental exposure to the patch by children, caregivers, or others (33 cases)
- Pharmacology-related errors
 - Withdrawal (158 cases)
 - Overdose (83 cases)
 - Cardiopulmonary arrest (32 cases)
 - Classic opioid side effects
 - Nausea (85 cases)
 - Vomiting (68 cases)

To address safety risks of long-acting opioids such as fentanyl patches, the Food and

Drug Administration (FDA) took the following actions:

- In July 2012, FDA mandated a Risk Evaluation and Mitigation Strategies Plan (REMS) to provide education and training on the safe use of opioids.
- In March 2013, FDA launched a [Safe Use Initiative](#) to increase public knowledge about how to safely use, store, and dispose of fentanyl (Duragesic) patches.
- In July 2013, FDA improved warnings in the product information for this drug class and required the conduct of post-marketing studies.
- In September 2013, FDA necessitated color changes for the text of fentanyl (Duragesic) patch labels for better visibility on the skin or if they have fallen off of the patient to assist in the prevention of accidental exposure to children, caregivers, pets, and others.

VA has been active in the education, tracking, and monitoring of safe and appropriate use of opioid analgesics since Fiscal Year (FY) 2002. Multidisciplinary groups coordinate education on appropriate pain management and assist in optimizing safe outcomes with opioid therapy. Development of new prescription monitoring tools is enabling the VA to track high dose opioid use and aberrant opioid use across the system nation-

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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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from the fda

INFECTIOUS DISEASE

[FDA warns of increased risk of death with IV antibacterial Tygacil \(tigecycline\) and approves new Boxed Warning](#)
9/27/2013

A new Boxed Warning and additional updates to product information (*Warnings and Precautions* and *Adverse Reactions* sections) will address the increased risk of death when intravenous (IV) tigecycline (Tygacil) is used for FDA-approved uses as well as for non-approved uses. Since 2010, FDA analyzed data from 10 clinical trials conducted solely on FDA-approved uses [complicated skin and skin structure infections (cSSSI), complicated intra-abdominal infections (cIAI), and community-acquired bacterial pneumonia (CABP)]. Results indicated greater risk of death in patients receiving tigecycline for approved uses [2.5% (66/2640)] compared to other antibacterial drugs [1.8% (48/2628)], with a 0.6% adjusted risk difference for death and corresponding 95% confidence interval of (0.0%, 1.2%). These deaths came about from infections (exacerbations and/or complications) or other underlying medical conditions. FDA recommends that health care professionals should reserve tigecycline for use in situations when alternative treatments are not suitable.

ONCOLOGY

[Boxed Warning and new recommendations to decrease risk of hepatitis B reactivation with the immune-suppressing and anti-cancer drugs Arzerra \(ofatumumab\) and Rituxan \(rituximab\)](#)

9/25/2013

Two anti-cancer drugs, ofatumumab (Arzerra) and rituximab (Rituxan), have immunosuppressive properties and bear risk of reactivation of Hepatitis B virus (HBV) infection in patients who have had prior HBV exposure. Some cases have resulted in fulminant hepatitis, hepatic failure, and death. Revised product information will describe the risk of HBV reactivation in the existing *Boxed Warning* of the rituximab (Rituxan) label and a new *Boxed Warning* for the ofatumumab (Arzerra) label. Updates to the *Warnings and Precautions* sections will recommend:

- Screening –
 - ◊ All patients should have hepatitis B surface antigen (HBsAg) and hepatitis B core antibody (anti-HBc) measured before starting treatment with ofatumumab (Arzerra) or rituximab (Rituxan).
- Monitoring –
 - ◊ Consult with hepatitis experts on monitoring and use of anti-viral therapy in patients at risk of HBV reactivation due to prior HBV infection.
 - ◊ Monitor patients with prior HBV infection for clinical and laboratory signs of hepatitis B or HBV reactivation during therapy with ofatumumab (Arzerra) or rituximab (Rituxan), as well as for several months after stopping therapy since HBV has been reported to occur up to 12 months following completion of therapy.
- Management –
 - ◊ Discontinue ofatumumab (Arzerra) or rituximab (Rituxan) and start appropriate treatment for HBV in patients who develop reactivation of HBV.
 - ◊ Discontinue other chemotherapy until the HBV infection is controlled or resolved.
 - ◊ No evidence supports resuming ofatumumab (Arzerra) or rituximab (Rituxan) in patients who develop HBV reactivation hepatitis.

PAIN MANAGEMENT

[FDA requiring color changes to Duragesic \(fentanyl\) pain patches to aid safety—emphasizing that accidental exposure to used patches can cause death](#)

9/23/2013

FDA mandates color changes on the writing of brand and generic fentanyl (Duragesic) patches for better visibility so that patients and caregivers can easily see and locate patches on patients' bodies, or those that have fallen off, to prevent accidental exposures. The current ink color varies by strength and is not always easy to see. Searches of surveillance databases from the FDA [from 1990 until 2012] and Centers for Disease Control (CDC) [from 2004-2010] identified 30 cases of pediatric accidental exposures occurring in either patient's homes or in health care settings where children followed adults to visit patients. Out of these 30 cases: 10 described serious harm resulting in death; 16 required hospitalization and medical intervention; 28 involved children ≤ 10 years of age; and 19 involved children ≤ 2 years of age. In September 2013, FDA reported 2 more pediatric deaths related to accidental exposure of fentanyl patches in children during the past 18 months. Causes of accidental exposure include improper disposal of the patch into the household trash and transfer of a patch to a child in close proximity.

Getting the most from our safety surveillance

OPPORTUNITIES TO PARTICIPATE IN VA SAFETY INITIATIVES

ATTENTION PHARMACISTS: CALL FOR PARTICIPANTS

Professional society guidelines recommend that the shortest duration of antimicrobial therapy appropriate to treat pneumonia should be prescribed. The appropriate duration of antibiotic therapy for pneumonia varies depending on the diagnosis, patient specific characteristics, and antimicrobial agent(s) used. However, shorter-course antimicrobial therapies may provide substantial benefits, including decreasing the spread of antibiotic resistance, improving patient compliance, reducing the risk of adverse effects including *Clostridium difficile* infection (CDI), shortening the length of hospitalization, and reducing cost.

VA PBM/VAMedSAFE, in collaboration with the VA Antimicrobial Stewardship Task Force, is conducting a national medication use evaluation (MUE) titled “**Total Duration of Antibiotic Therapy for Veterans Hospitalized with Pneumonia**” in order to determine if prescribing practices are consistent with practice guideline recommendations for length of therapy. We are soliciting participation from 20-25 geographically dispersed VA medical centers for involvement in the quality assurance

(QA)/quality improvement (QI) initiative. Sites expressing interest will need to register this operations activity with local QA/QI governing bodies according to standard operating procedures. Should sites choose to conduct this evaluation as a local research project, then local IRB review and approval would be essential.

Anticipated commitment for participation:

- Complete paperwork (Data Use Agreement)
- Attend monthly conference calls
- Conduct chart review (approx. 150-200 charts depending on size of facility; final number pending)
- Respond to post data collection questions during data cleaning process

Please reply to **Melinda Neuhauser** (Melinda.Neuhauser@va.gov) and **Muriel Burk** (Muriel.Burk@va.gov) if interested.

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CONTINUING SAFETY RISKS WITH FENTANYL PATCHES

(continued from page 1)

wide. VA will continue to address new risks with this drug class as they continue to be identified by FDA, ISMP, and internally within the VA.

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