



# Pharmacy Benefits Management- Medical Advisory Panel E<sub>z</sub>-Minutes

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**PLEASE NOTE:** The PBM web site has had an extreme makeover! Check out our brand **NEW** web design. Also, please note our **NEW** web addresses. Take a second and visit us at <http://www.pbm.va.gov> or <http://vaww.pbm.va.gov>. **Be sure** to bookmark the **NEW** addresses.

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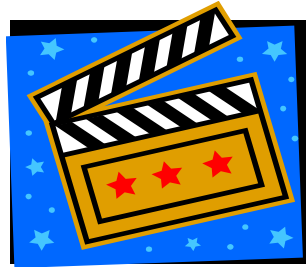
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## COX-2 Recall: Take 2

**Background:** On April 7<sup>th</sup>, 2005 valdecoxib (Bextra®) was withdrawn from U.S. markets. After careful review of the available data, the Food and Drug Administration (FDA) concluded that the risks of valdecoxib may outweigh the benefits and requested that the manufacture, Pfizer, withdraw valdecoxib. Pfizer has agreed to stop the sales and marketing of their product "pending further discussions" with the FDA. The FDA cited several reasons to support their request for withdrawal including a lack of adequate long-term cardiovascular safety data for valdecoxib; an increased risk of cardiovascular events observed during short-term use in patients after coronary artery bypass surgery (CABG); serious and unpredictable life-threatening skin reactions; and finally a lack of evidence to support an advantage of valdecoxib compared with other nonselective NSAIDs. Please refer to <http://www.fda.gov/cder/drug/advisory/COX2.htm> for additional information.

**What actions have been taken by the PBM-MAP?**

1. In October 2004, the PBM-MAP distributed an electronic bulletin recommending that valdecoxib be avoided until more conclusive data were obtained with regard to risk of cardiovascular events.
2. In January 2005, the PBM-MAP created additional guidance regarding the COX-2 inhibitors and nonselective NSAIDs. Please refer to [http://vaww.pbm.va.gov/clinicians/COX-2\\_guidance.pdf](http://vaww.pbm.va.gov/clinicians/COX-2_guidance.pdf). Recommendations were made at that time to switch all valdecoxib users to alternative treatments and that no new patients receive valdecoxib.
3. Additional information and guidance for clinicians regarding switching current users is available on <http://vaww.pbm.va.gov/vioxx/Voluntary%20Withdrawal%20of%20Valdecoxib-guidance-Final%202005.pdf>
4. To assist you in communicating with your patients, the PBM has developed a Valdecoxib Patient Switch Letter. Click on <http://vaww.pbm.va.gov/vioxx/Valdecoxib%20switch-patient%20letter.pdf>.

**Please Note:** As of April 11<sup>th</sup>, 2005, all VA facilities should have already discontinued prescribing and dispensing valdecoxib.

## ***Another Drug Recall---- natalizumab (Tysarbi®)***

**On February 28, 2005, natalizumab (Tysarbi®) was voluntarily withdrawn from the market by its manufacturers, Biogen-Idec and Elan. This was in response to adverse events involving reports of one fatal, confirmed case and one suspected case of progressive multifocal leukoencephalopathy (PML). PML is a rare and frequently fatal, demyelinating disease of the central nervous system. Subsequently on March 30, 2005, it was announced that a previously diagnosed case of malignant astrocytoma had been reevaluated as PML, in a patient participating in an open label Crohn's disease clinical trial.**

**The PBM and VAMedSafe have worked with VISN Formulary Leaders in identifying all patients receiving natalizumab therapy. A survey for each patient has been completed and will be reviewed by the PBM. Directions regarding the return of unused product have been provided to facilities including chiefs of pharmacy, VSIN Formulary Leaders, Medical Advisory Panel members, and clinical pharmacist mail group. *All therapy with natalizumab should be discontinued.***

### **ACTIONS FROM THE NATIONAL DRUG FILE (NDF) SUPPORT GROUP REGARDING ORAL ERYTHROMYCIN**

**In light of the findings from the following article, Oral Erythromycin and the Risk of Death from Cardiac Causes, (N Engl J Med 2004; 351; 1089-96), the NDF Support Group has discussed the classification of QTc pharmacodynamic (PD) drug interactions and agreed on the following: 1) If the package insert (PI) contains a Black Box Warning or the Medical Advisory Panel (MAP) guidelines contraindicate it, then the national severity for the interaction will be CRITICAL. 2) If the PI or MAP has as a precaution or warning then the severity is SIGNIFICANT. 3) If there is a pharmacokinetic and pharmacodynamic (PD) interaction, depending on the amount of level increase and the propensity of the drug to cause a QTc prolongation, the severity will be SIGNIFICANT or CRITICAL, and 4) If PD information is only available and no clinical data exists to support the severity or extent of the interaction, the interaction will not be added to the file.**

### **Name change for Reminyl®**

**There have been recent reports of dispensing errors due to confusion with the names of the diabetes drug AMARYL® (glimepiride) and REMINYL® (galantamine HBr). The manufacturer has received FDA approval to change the name of the product to RAZADYNE™ (galantamine HBr). This name will apply to the immediate release form and the extended release for which will become available in May 2005.**

### **CONTRACT REVIEW**

**The national award for the angiotensin II receptor antagonist is for losartan for patients with type 2 diabetic nephropathy. The award for the angiotensin II receptor for patients with systolic heart failure is pending. Additional information regarding the angiotensin II receptor antagonist for systolic heart failure will be forthcoming. Criteria for Use for the angiotensin II receptor antagonist were recently posted and are available at the following website: <http://www.pbm.va.gov/PBM/treatment.htm>.**

## Recent National PBM Reviews Postings on Web Site Criteria for Use

<http://www.pbm.va.gov/PBM/criteria.htm>

Cilostazol (Pletal®)

The Angiotensin II Receptor Antagonist Criteria

## Drug Monographs

<http://www.pbm.va.gov/PBM/drugmonograph.htm>

Cilostazol (Pletal®)

Duloxetine (Cymbalta)-in painful Diabetic Neuropathy and  
Fibromyalgia

Rifaximin (Xifaxan™)

Telithromycin (Ketek™)

## New Molecular Entities Review

**Tinidazole (Tindamax®)-  
Not added to VANF or  
VISN Formularies**

**Rifaximin (Xifaxan®)-Not  
added to VANF or VISN  
Formularies**

## Initial Selection of SSRI Algorithm for Primary Care Updated

The availability of generic citalopram has resulted in changes to the algorithm for the initial selection of selective serotonin reuptake inhibitors (SSRIs) in primary care. Citalopram is now considered one of the preferred SSRIs in the VA Healthcare System along with fluoxetine and paroxetine. Mirtazepine, a non-SSRI antidepressant, is also on this list. Citalopram provides an alternative to fluoxetine and paroxetine for patients for whom the prescriber is concerned about drug-drug interactions involving the cytochrome P450 2D6 or 3A4 isozymes, fluoxetine's long half-life, or paroxetine's anticholinergic effects.

Prescribers are encouraged to reserve non-preferred antidepressants for patients that have failed to respond to at least one of the preferred antidepressants, who have indications not covered by the preferred antidepressants, or who have contraindications to the preferred antidepressants.

Justification for the initial use of the preferred antidepressants is largely driven by their generic availability and cost, and the finding that overall all antidepressants have similar efficacy response rates in clinical trials. With the exception of fluvoxamine, the other SSRIs are indicated for treating major depressive disorder and at least one of the anxiety disorders.

### Direct Cost Comparison of VA Preferred First-Line Antidepressants

	Citalopram	Fluoxetine	Paroxetine	Mirtazapine
Daily Dosage Range	10 - 40 mg	10 - 40 mg	10 - 40 mg	15 - 45 mg
Cost per tab/cap/day*	\$0.08 - 0.09	\$0.03 - 0.06	\$0.30 - 0.90	\$0.13 - 0.39

\*Costs estimated using tablet-splitting whenever possible; fluoxetine, paroxetine, and mirtazapine costs based on generic pricing.

### Alternative First-Line Antidepressants

	Sertraline	Bupropion (generic)	Bupropion SA (generic)	Venlafaxine XR
Daily Dosage Range	50 - 200 mg	100 - 400 mg	100 - 400 mg	75 - 300 mg
Cost per tab/cap/day*	\$1.20 - 2.48	\$0.14 - 0.64	\$0.69 - 2.18	\$1.73 - 3.78

For additional information and the updated algorithm see <http://www.pbm.va.gov/guidelines/SSRI%20Algorithm.pdf>

Submitted by Todd Semla, MS, PharmD, BCPS, FCCP

## **PBM-MAP DISTANCE LEARNING BROADCAST PROGRAMS**

### **Challenges and Treatment Options for Metabolic Changes Seen in Patients with Mental Illness**

The program is scheduled to air on June 29, 2005 at 1 p.m. Eastern Time. Immediately following the conclusion of the program, there will be a Q/A time with the faculty and colleagues. Check the web site <http://www.pbm.va.gov/PBM/dislearning.htm> in the near future for the dial-in number. The program will rebroadcast on the following dates: July 1, 2005, 11:00 a.m. (ET); July 5, 2005, 8:00 p.m. (ET); July 14, 2005, 2:00 a.m. (ET); July 18, 2005, Noon (ET).

### **Clinical Update on the Management of Benign Prostatic Hypertrophy**

This program is scheduled to air on August 3rd at 1 p.m. Eastern Time. A live Q/A period will follow the conclusion of the program. The rebroadcast dates and times are: August 5, 2005, 11 a.m. (ET), August 9<sup>th</sup>, 2005, 8 p.m. (ET), August 18<sup>th</sup>, 2005, 2 a.m. (ET), and August 26<sup>th</sup>, 12 Noon (ET).

More details when available will be posted on the web site. Be sure to click on <http://www.pbm.va.gov/PBM/dislearning.htm>.

## **VAMedSAFE Ethyl Chloride Ignites!**

### **What's Ethyl Chloride?**

Ethyl chloride is a topical anesthetic skin refrigerant and is used to 1) control pain associated with injections, minor surgical procedures, and the temporary relief of minor sports injuries; 2) treat restricted motion associated with myofascial pain caused by trigger points; and 3) test for the vitality of tooth pulp in dentistry. Over-application may alter skin pigmentation, especially with dark complexions and can take months to return to normal. Ethyl chloride's anesthetic effects rarely last longer than a minute.

### **How does it Ignite?**

Fires are started when the three elements of the fire triangle are present – heat, fuel, and oxygen. Of more than 23 million inpatient surgeries and 27 million outpatient surgeries performed each year, it has been estimated that approximately 100 surgical fires occur each year, resulting in up to 20 serious injuries and one or two patient deaths annually.<sup>1-3</sup> Most common ignition sources are electrosurgical equipment (68%) and lasers (13%). Ethyl Chloride is an agent that is flammable around heat sources and has recently been cited as a culprit in the cause of several patient-related fires in physicians' offices. Contrary to popular belief, it is not necessary for the spray to be in close proximity to the source of ignition, like a spark or cautery device, in order for it to ignite. This is because the weight of ethyl chloride vapors is heavier than air. Therefore, the vapors can sink to the floor and travel away to another area, potentially allowing for ignition to occur at a distant source. However, a sudden flashback can occur, whereby the flames are swept back to the person on whom ethyl chloride is being applied.

### **Cases in the Literature**

Case 1: In preparation to treat a 6-year-old child's infected toe, ethyl chloride was sprayed to numb the area before lancing with surgical cautery. Upon triggering the device, the entire surgical area ignited into flames, including the pad beneath the child's foot.

Case 2: Ethyl chloride was sprayed on a girl's forehead in preparation for an abscess drainage. While waiting for it to dry, the health professional turned on the cautery device and proceeded to perform the drainage. The patient was wearing a flammable synthetic wig due to hair loss, and the wig ignited upon application of the heat source to her forehead. The patient sustained first-degree burns to her ear.

### **Are there other agents that can cause this?**

Yes. Other commonly used medical products have been reported as causes in surgical fires as well: prepping agents containing alcohol, eye lubricants (LACRI-LUBE S.O.P.), ointments, and wound dressings (tincture of benzoin and collodion), are some examples.

### **What Is Recommended? - From the Institute for Safe Medication Practices (ISMP).**

1. Inform all healthcare workers on the dangers of flammable products such as ethyl chloride, realizing the potential for burns when these products are used with a heat source.
2. Facilities should re-evaluate the need for flammable products, and explore safer alternatives for topical anesthetics

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## What are the recommendations from the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) to help health care organizations prevent surgical fires?

1. Educate staff members on the importance of controlling heat sources by following laser and electrosurgical units (ESU) safety practices; managing fuels by allowing sufficient patient prep time; and establishing guidelines for minimizing oxygen concentration under drapes. Free educational posters on surgical fires are available at: [www.mdsr.ecri.org/asp/dynadoc.asp?id=195&nbr=413558](http://www.mdsr.ecri.org/asp/dynadoc.asp?id=195&nbr=413558)
2. Developing, implementing, and testing procedures to ensure appropriate response by all staff members to fires in the operating room.
3. Report any instances of surgical fires as a means of raising awareness and ultimately preventing the occurrence of fires in the future.

### **PLEASE NOTE:**

- The labels on ethyl chloride containers have poorly visible warnings about flammability because they are set in a small type size. The flame icon indicating its flammability appears more like a flower. Facilities should add an auxiliary label to warn about flammability before such products are dispensed to various units in the facility.



**Alternatives: Gebauer, the leading manufacturer of ethyl chloride has introduced non-flammable alternatives to ethyl chloride**

#### **1. Ethyl Chloride and Dichlorotetrafluoroethan (Fluro-Ethyl®)**

A vapocoolant used for pain control associated with minor surgical procedures (lancing boils, incisions, drainage of abscesses, sutures), dermabrasion, injections and minor sports injuries. Use is contraindicated in patients with vascular impairment of extremities. Over-application may alter skin pigmentation, especially with dark complexions and can take months to return to normal. Fluro-Ethyl® is NON-FLAMMABLE but contains chlorofluorocarbons which can deplete the ozone. It should be stored in a cool place (under 120° F). Fluro-Ethyl's® anesthetic effects rarely last longer than a minute. The McKesson VA price is \$17.37/5.0 oz (AWP Red Book \$22.20)

#### **2. 1,1,1,3,3-Pentafluoropropane/1,1,1,2 Tetrafluoroethane (Pain Ease®)**

A vapocoolant used for pain associated with injections, minor surgical procedures (lancing boils, incisions, drainage of abscesses, sutures), temporary relief of minor sport injuries, and as a counterirritant in the management of myofascial pain, restricted motion and muscle tension. Use is contraindicated in patients with diabetes and poor circulation. Over-application may alter skin pigmentation, especially with dark complexions and can take months to return to normal. Pain Ease® is NON-FLAMMABLE and non-ozone depleting. It should be stored in a cool place (under 120° F). Pain Ease's® anesthetic effects rarely last longer than a minute. The AWP (Amerisource, February 2005) for Pain Ease® is \$22.19 per can. This item is not currently stocked by McKesson.

### **Conclusion:**

**Most, if not all, surgical fires are preventable, and their impact can be mitigated through an understanding of fire and knowledge of the safe handling of flammable healthcare products. VA MedSAFE supports the recommendations of ISMP and JCAHO for staff education, clearer warning labels, and as well as consideration of safer alternatives.**

### **References:**

1. Hall MJ, Owngs MF. 2000 National Hospital Discharge Survey. Advance data from vital and health statistics; No 329. Hyattsville, Maryland: National Center for Health Statistics. 2002.
2. Hall MJ, Lawrence L. Ambulatory surgery in the United States, 1996. Advance data from vital and health statistics; no. 300. Hyattsville, Maryland: National Center for Health Statistics. 1998.
3. ECRI. A clinician's guide to surgical fires: how they occur, how to prevent them, how to put them out (guidance article). Health Devices 2003; 32(1):5-24.

### **Additional Information Sources:**

ISMP Medication Safety Alert: Extreme caution needed with flammable products. March 11, 2004. <http://www.ismp.org/MSAarticles/extreme.htm>  
ISMP Medication Safety Alert: Ethyl chloride ignites. August 26, 2004. <http://www.ismp.org/MSAarticles/ethyl.htm>  
JCAHO Sentinel Even Alert [http://www.jcaho.org/about+us/news+letters/sentinel+event+alert/sea\\_29.htm](http://www.jcaho.org/about+us/news+letters/sentinel+event+alert/sea_29.htm)

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