

# pmsinfo

*A quarterly publication of PMSI Clinical Services*

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We are excited to bring you another edition of *PMSInfo*, our quarterly newsletter that compiles and delivers important industry information regarding medication trends, utilization management, pharmaceutical issues, clinical studies, and more. In this issue, we are introducing clinical topics related to durable medical equipment and specialty services, as our clinical nurse consultants were recently incorporated into our Clinical Services team. This addition will bring deeper insight regarding medical services trends, equipment utilization, and new products in the marketplace, etc. Our end goal is to provide a source of knowledge that can be used every day as you work through all phases of the injury lifecycle. We hope you enjoy this enhancement and find the new content valuable. Please let us know your thoughts by e-mailing [clinical@pmsionline.com](mailto:clinical@pmsionline.com).

Maria Sciamè, PharmD, CDE, RRT  
Director of Clinical Services

## Drug Recalls: 101

Recent prescription drug recalls have left many questioning the safety of medications on the U.S. market. The goal of this article is to highlight the drug recall process and emphasize the role of the pharmacy in situations where a patient may have received a recalled product.

The purpose of the Food and Drug Administration (FDA) is to provide regulation and oversight into the introduction of medications, foods, biological products, and other products intended for human consumption. The FDA's main focus is to ensure that products are safe and effective for the end user as well as to ensure balanced representation by drug manufacturers of the drugs' intended use and efficacy. As a consequence, drug manufacturers are mandated to report any post-marketing observations of adverse drug reactions to the FDA, either from internal analyses or as a result of notification from an end user or healthcare professional.

When patient safety is a concern, the FDA, in conjunction with drug manufacturers, conducts drug recalls in an attempt to limit the exposure of potentially harmful medications to end users. These drug recalls serve to protect the public from medications that are deemed to be potentially harmful to humans.

The FDA uses the Adverse Event Reporting System (AERS) to quickly assess the severity and anticipated human impact of the alleged drug-related problem(s). In rare cases where a product must be removed from the market, a recall severity scale detailing the impact to human health is utilized. This recall scale, ranging in severity from a high probability to cause human harm/death (Class I) to not likely to cause human harm/death (Class III) is communicated to drug manufacturers and the public via direct FDA correspondence as well as postings on the FDA's website at <http://www.fda.gov/opacom/Enforce.html>.

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### The PMSI Mail Order Pharmacy Recall Process

The National Association of Boards of Pharmacy® (NABP®) Model State Pharmacy Act established that pharmacies have the responsibility to “...develop and implement a procedure for proper management of drug recalls, which may include, where appropriate, contacting patients to whom the recalled drug product(s) have been dispensed.”

With health and safety paramount, PMSI is dedicated to protecting injured workers from medications that may be part of a medication recall. Our process involves three main actions: sequestering of inventory, risk assessment, and patient updates. Once a recall notice is received, PMSI removes any unused inventory from our pharmacy and arranges for it to be returned to the manufacturer. Our state-of-the-art automated dispensing system, in collaboration with documented receiving procedures, enables the identification of currently affected and previously dispensed stock. In the event that affected medications have been dispensed, a call plan is enacted to alert the injured worker as to the severity and cause of the recall and to ensure that the provider has an opportunity to intervene in the event that any adverse medication reactions have been

experienced. Resolution often involves advising injured workers to contact their physicians for re-issuance of medication orders. Prescriptions marked as “re-issued” due to recalls are adjudicated as such to ensure that they do not show up as duplicate transactions during billing. Once recalls are completed, PMSI retains all documentation pertaining to the recall process as well as injured worker notifications for future reference.

As your partner, PMSI will continue to monitor FDA updates and manufacturer communications to ensure that injured workers receive the safest, most effective medications possible. PMSI has and continues to handle all medication recalls with vigilance and swiftness of action. At PMSI, nothing is more important than the health and well-being of our injured workers.

References: Food and Drug Administration web site: [www.fda.gov](http://www.fda.gov). <Accessed January 15, 2009>. National Association of Boards of Pharmacy® web site: [www.nabp.net](http://www.nabp.net). <Accessed January 15, 2009>

[See the FDA MedWatch section for the latest drug recalls.](#)

## NEW! *clinical nursing news*

### The Role of the Workers' Compensation Case Manager

Case managers play a vital part in the life of a workers' compensation claim. They wear many hats, such as coordinator, facilitator, advocate, and educator. Oftentimes their responsibilities are varied depending on the employer, background and certifications, which can lead to confusion among claims professionals. To better understand this important role, let's take a closer look at the value they bring to all involved, some of the common types of case managers, and how PMSI partners with case managers to improve outcomes.

#### Value

Case managers assist in meeting the complex needs of all parties within a case. Depending on the circumstances, a case manager may interact in the following manner with an individual/group:

**Carrier/TPA/Claims Adjustor:** Assists in medical care coordination providing the maximum cost benefit, clarifies medical information to the lay person (i.e., claims examiner), and coordinates all care.

**Employee:** Empowers injured workers by giving them and their families a better understanding of their disability, illness or disease, provides a greater voice in the delivery of their healthcare, and serves as an advocate.

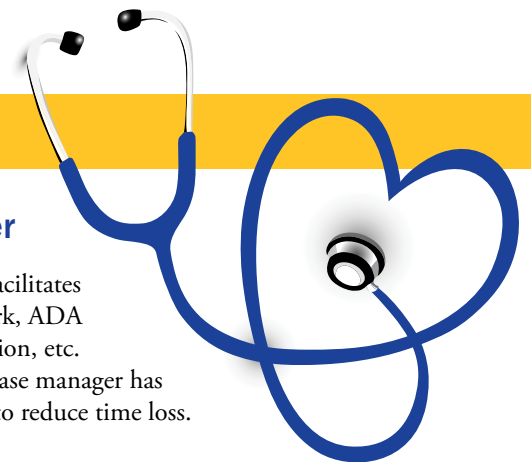
**Employer:** Facilitates return to work, ADA accommodation, etc. Assigning a case manager has been shown to reduce time loss.

#### Roles

In the multifaceted case management industry, case managers work in a variety of roles; they are usually nurses, social workers or rehabilitation counselors. A workers' compensation case manager typically requires several years of experience in Orthopedics, Med Surgical, or Rehabilitation. These prerequisites are valuable, as most workers' compensation injuries are musculoskeletal in nature.

The most common role in workers' compensation is the **Field Case Manager or FCM**. They typically work from a home office and carry a case load of 20 to 40 files. FCMs are primarily responsible for coordinating medical care using the most cost beneficial approach, projecting cost of care, facilitating return to work, and establishing and following short- and long-term goals until the injured worker has reached maximum medical improvement (MMI). The FCM works in the field, attends injured worker appointments, meets with physicians and other healthcare providers.

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## The Role of the Workers' Compensation Case Manager

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The **Telephonic Case Manager** performs similar functions as the FCM but conducts all business via office telephone.

The **Utilization Review Nurse (UR nurse)** is a case manager who ensures treatment follows standard medical guidelines (e.g., ACOEM in California). They review medical information on a retrospective, prospective or concurrent basis to provide authorization for medical treatment or recommendations for alternative therapy (with physician advisor review or standards as established by state guidelines).

In addition, the Commission for Case Manager Certification offers credentials for all types of case management roles. This designation is called a **Certified Case Manager (CCM)** and requires a combination of work experience, education and examination.

## Partnerships

PMSI works closely with workers' compensation case managers to achieve a common goal of enhancing injured worker outcomes. PMSI's Clinical Nurse Consultants work with case managers to understand the needs of the injured worker, research available options, recommend the most cost-effective choices for medical supplies and equipment, and coordinate care and services from multiple providers. Working with PMSI saves a busy case manager valuable time, provides cost savings, reduces risk, and frees them up to focus on other critical tasks.

For more detailed information about case management, go to [www.ccmcertification.org](http://www.ccmcertification.org).

## features

### Eli Lilly Will Resubmit Supplemental New Drug Application for Cymbalta for Pain Control

Pharmaceutical giant Eli Lilly and Company has decided to resubmit its request to the FDA for their antidepressant agent, Cymbalta® (duloxetine), to include the treatment of osteoarthritis knee pain. This resubmission comes as a result of recent clinical trials conducted by Eli Lilly showing potential benefits for arthritis patients. Previously, Eli Lilly decided to withdraw its request for an expanded indication after FDA reviewers questioned the statistical design and line of attack of other clinical studies and were concerned about reported efficacy and dosing recommendations. "This was a difficult decision, but we believe the updated data package will give the FDA a broader basis for reviewing our application," stated John Hayes, a member of Eli Lilly's Research Laboratory leadership team. The company plans to submit the supplemental new drug application (sNDA) in early 2009 with data from recent clinical trials indicating positive outcomes in knee osteoarthritis sufferers. Although data from these clinical trials appears promising, the true clinical advantage of Cymbalta over already available products for osteoarthritis knee pain, some of which are available as generic equivalents, remains to be seen. Due to a fairly limited occurrence of compensable osteoarthritis knee pain in most workers' compensation cases, it is suspected that this potential change in use may have a limited impact in the workers' compensation market. Cymbalta is currently only FDA approved for the treatment of anxiety, depression, diabetic neuropathy, and fibromyalgia.

Reference: *Eli Lilly and Company Pulls FDA Application for Cymbalta for Pain.* [http://www.lifescience-online.com/Eli\\_Lilly\\_and\\_Company\\_Pulls\\_FDA\\_Application\\_for\\_Cy,13068.html?portalPage=Lifescience+Today.News](http://www.lifescience-online.com/Eli_Lilly_and_Company_Pulls_FDA_Application_for_Cy,13068.html?portalPage=Lifescience+Today.News) <Accessed December 5, 2008>

### Clinical Trials for Relistor in Non-Cancer Pain-Related Opioid-Induced Constipation Achieve Primary and Secondary Endpoints

As of late 2008, Wyeth Pharmaceuticals announced that its clinical trial assessing the efficacy of Relistor® (methylnaltrexone) for opioid-induced constipation in chronic, non-cancer-related pain reached expected primary and secondary endpoints. Relistor was approved in spring 2008 as a treatment for opioid-induced constipation in cancer patients unmanaged with standard laxative therapy; however, Wyeth Pharmaceuticals wants to expand this indication for use in chronic, non-cancer pain patients. "Many patients who take prescription opioids to help relieve their non-cancer pain experience opioid-induced constipation, which can disrupt their lives," commented Gary Stiles, M.D., Chief Medical Officer for Wyeth Pharmaceuticals. "This phase 3 clinical study of Relistor subcutaneous injection showed statistically significant improvements in the occurrence of bowel movements in patients with opioid-induced constipation who have chronic, non-cancer pain." Although the study suggests that Relistor may be effective for this patient population, it is yet to be determined if a clinical advantage will be observed when other factors such as ease of administration, cost, and duration of therapy (studies assessing efficacy beyond four months are unavailable) are considered, especially when taking into account the chronic nature of opioid-induced constipation. Due to the use of opioid analgesics in injured workers, opioid-induced constipation continues to be an ongoing concern. If Relistor receives FDA approval for additional types of constipation treatments, this could translate into a significant increase in total spend for injured workers with chronic pain.

Reference: *Wyeth and Progenics Announce Positive Outcome of Phase 3 Clinical Study of Subcutaneous Relistor for Opioid-Induced Constipation in Patients with Chronic Non-Cancer Pain.* Wyeth Pharmaceuticals. <http://news.moneycentral.msn.com/ticker/article.aspx?Feed=BW&Date=20081126&ID=9408843&Symbol=PGNX>. <Accessed January 15, 2009>

# clinical literature digest studies

## STUDY #1: Topical NSAIDs for Chronic Musculoskeletal Pain: Systemic Review and Meta-analysis

Musculoskeletal pain is associated with injury to the musculoskeletal system (bones, muscles, tendons, ligaments, joints, cartilage, and other connective tissue), and is a common symptom reported to clinicians by injured workers. Non-steroidal anti-inflammatory agents (NSAIDs) are universally utilized to treat pain and inflammation resulting from musculoskeletal injuries. Although efficacy is well documented with this category of medications, concerns regarding systemic gastrointestinal (i.e., GI bleeding, ulcer, and perforation) and cardiovascular (i.e., edema, hypertension, and heart failure) adverse effects can be a major concern. It is perceived that agents that are applied locally to an injured area to treat symptoms may reduce the risk of systemic adverse effects in comparison to their oral counterparts.

This review evaluates the efficacy and safety of topical NSAIDs for chronic musculoskeletal pain. The review identified reports of randomized, double-blind, active or placebo-controlled trials in which treatments were given to adult patients with moderate-to-severe chronic pain resulting from musculoskeletal or other painful disorders. Clinical success was defined as approximately a 50% reduction in pain at two weeks. Topical NSAIDs that were used in the active-controlled trials included piroxicam 0.5% gel, diclofenac 1% gel, and eltenac 1% gel; oral formulations were ibuprofen 1200mg per day and diclofenac 100mg per day. In the placebo-controlled trials, the mean placebo response rate was 26% in comparison to the mean treatment response rate of 48%. In the active-controlled trials comparing topical NSAIDs with oral NSAIDs, there was no statistically significant difference; both formulations reported 37% successful outcomes.

This review also evaluated the safety of topical NSAIDs. There was no statistically significant difference between injured individuals receiving topical NSAIDs and topical placebo. Both groups reported experiencing local adverse events of 6%, systemic adverse events of 3%, or withdrawal from the trial due to an adverse event of 1%. In the active-controlled trials comparing topical with oral NSAIDs,

local adverse events occurred more frequently with topical NSAIDs at 8%, versus oral NSAIDs at 3%. Systemic adverse events and withdrawal from trials as a result of adverse events did not differ between topical and oral NSAIDs. No study documented specific instances of upper gastrointestinal bleeding or symptomatic ulcers. This review suggests that topical NSAIDs may be equally effective as oral NSAIDs; however, topical NSAIDs may not offer any additional systemic benefits compared to the oral formulations.

Mason L, Moore RA, Edwards JE, Derry S, McQuay HJ. *Topical NSAIDs for Chronic Musculoskeletal Pain: Systematic Review and Meta-analysis*. BMC Musculoskeletal Disorders. 2004 Aug 19; 5:28.

## STUDY #2: Patterns of Abuse Among Unintentional Pharmaceutical Overdose Fatalities

Clinicians have an arduous task of attempting to balance the duty of relieving pain experienced by their patients and being responsible in helping to prevent the broader health problems of addiction and overdose death. There has been enormous national attention to encourage clinicians to utilize the broad range of agents available to relieve pain. However, prescribers are fully aware that there has been an increase in injuries and deaths associated with pain relievers, in particular with the use of opioids. Opioid abuse has developed into a national public health threat.

The objective of this study was to characterize persons dying of drug overdoses in West Virginia in 2006 with regard to potential risk factors and the types of drugs that resulted in their deaths. This study identified all state residents who died of unintentional drug overdose in West Virginia in 2006. Decedents were included if their death certificates listed the underlying cause of death to be unintentional drug poisoning, ICD-10 codes X40-X44. Cases were initially identified by searching an electronic database of vital records at the Health Statistics Center of the West Virginia Department of Health and Human Resources using the appropriate ICD-10 codes. This information was cross-referenced with the case logbook and electronic database of the investigations of the Office of the Chief Medical Examiner.

Results showed that of 295 decedents, 67.1% were men and 91.9% were between the ages of 18 and 54. Significantly greater death rates were observed among divorced and never-married decedents, 49.7 and 26.3 per 100,000 population, respectively, compared with married decedents, 12.3 per 100,000 population. Lower educational attainment and increased poverty in the decedent's county of residence were both associated with greater death rates. Pharmaceutical diversion was associated with 63.1% of deaths, while 21.4% were accompanied by evidence of doctor shopping (multiple prescribers). Opioid analgesics were taken by 93.2% of decedents. The most common drug identified contributing to death was methadone in 40% of the cases, followed by hydrocodone and oxycodone, 22.7% and 20.7%, respectively. The percentage of decedents with valid prescriptions for methadone was 32.1%, compared to decedents with valid prescriptions for hydrocodone (85.1%) or oxycodone (60.7%). When hydrocodone was the contributory prescription drug associated with an unintentional overdose, 83.6% of the decedents also utilized other prescription drugs. Studies that reveal patterns and trends of unintentional pharmaceutical overdose fatalities can provide helpful information that may be used to develop healthcare programs (such as alerting physicians that their patient is utilizing multiple prescribers) to assist in curbing this public health threat.

Hall A, Logan J, Toblin R, Kaplan J, Kraner J, Bixler D, Crosby A, Paulozzi L. *Patterns of Abuse Among Unintentional Pharmaceutical Overdose Fatalities*. JAMA. 2008 Dec 10; 300(22):2613-20

# FDA update

## New Drug Approvals

### Tapentadol

*Approved: November 2008*

The FDA approved **tapentadol**, the newest member to join the central-acting analgesic drug class late last year. Similar to tramadol (Ultram®), tapentadol works via a dual mechanism of action, acting on both mu receptors and inhibiting norepinephrine reuptake. Although clinical studies did reveal significant pain relief as compared to placebo, the efficacy of this agent compared to generically available tramadol is yet to be determined. A scheduled release date has not yet been announced pending review by the U.S. Drug Enforcement Agency and development of an official trade name.

## Generic Drug Arrivals

### Keppra® (levetiracetam)

*Launched: November 2008*

The once brand-only anticonvulsant agent, **Keppra**, is now available as the generic equivalent, levetiracetam. Normally utilized for the treatment of various seizure disorders, limited data has suggested the possible use of levetiracetam in the treatment of neuropathic pain. However, further clinical trials will need to be conducted in order to assess the true clinical significance of this intended indication. The new generic equivalent is currently available as a 250 mg, 500 mg, and 750 mg tablet.

### Imitrex® (sumatriptan)

*Launched: November 2008*

Released in late 2008, **sumatriptan** injection and tablets becomes the first triptan agent available as a generic equivalent for **Imitrex**. The drug is used for treatment of migraine headaches with and without aura as well as cluster headache pain relief. Imitrex nasal spray has also become generically available as of mid-December 2008.

### Depakote ER® (divalproex)

*Launched: January 2009*

**Depakote ER** has recently become generically available as of early 2009. Although originally approved for seizure disorders divalproex is utilized in a number of indications including migraine prophylaxis and bipolar disorder. Divalproex extended release is currently available in 250 mg and 500 mg tablet form.

## Anticipated Generic Drug Arrivals

### Ambien CR® (zolpidem)

*Anticipated Launch: First Quarter 2009*

**Ambien CR** is expected to become generically available in first quarter 2009 joining regular release Ambien (zolpidem) as one of the most popular prescription sedative-hypnotic agents on the market. Ambien CR is currently available in 6.25 mg and 12.5 mg tablet form.



# FDA MedWatch Reports

Highlighting Important  
Safety Issues from the FDA



## Medications Recalled Due to Higher-Than-Expected Active Drug Content

*Posted: 11/10/2008* — ETHEX Corporation and FDA notified healthcare professionals of a voluntary recall of five generic products including: propafenone HCl tablets, isosorbide mononitrate extended release tablets, morphine sulfate extended release tablets, morphine sulfate immediate release tablets, and dextroamphetamine sulfate tablets. The products were recalled because they may contain oversized tablets. Oversized tablets may contain more than the intended levels of the active drug ingredient that could result in patients receiving as much as twice the expected dosage of these drugs, which could cause serious or life-threatening consequences.

Overdoses can include arrhythmia and low blood pressure with propafenone HCl, fainting and low blood pressure with isosorbide mononitrate, respiratory depression and low blood pressure with morphine sulfate, and rapid heart rate and high blood pressure with dextroamphetamine sulfate. Patients who experience any adverse reactions to these drugs should contact their healthcare professional immediately. See the manufacturer's recall notice for specific lot numbers of the products affected by this recall.

Reference: FDA *MedWatch* Report. <http://www.fda.gov/medwatch/safety/2008/safety08.htm> <Accessed January 14, 2009>

## Hydromorphone 2 mg Recall

*Posted: 12/24/2008* — ETHEX Corporation and FDA notified healthcare professionals of a nationwide recall of a single lot of hydromorphone HCl 2 mg tablets due to potential for oversized tablets. Hydromorphone is a drug used for pain management. If someone were to take a higher-than-expected dose of hydromorphone, the risk of adverse effects known to be associated with the drug may be increased, including respiratory depression (difficulty or lack of breathing), low blood pressure, and sedation. The recalled tablets are a blue, round tablet with a script "E" on one side and a "2" on the other side.

The parent company of ETHEX Corporation, KV Pharmaceutical, has advised FDA that it is voluntarily suspending shipments of all FDA-approved drug products in tablet form. This action is being taken as a precautionary measure, to allow KV to address manufacturing issues that have come to the management's attention.

Reference: FDA *MedWatch* Report. <http://www.fda.gov/medwatch/safety/2008/safety08.htm> <Accessed January 14, 2009>

Patients who suspect that their prescriptions have been affected by lots of the medications involved in these voluntary recalls should contact the pharmacy where the prescriptions were dispensed. The dispensing pharmacy will handle affected prescriptions on a case-by-case basis.



PMSI—The Only Solution You Need.

Founded in 1976, today PMSI is one of the nation's largest providers of specialty managed care services and products for the workers' compensation and liability markets. PMSI provides a best-in-class integrated portfolio of services in Pharmacy, Settlement Solutions, Medical Services and Equipment, and Clinical Services that promotes quality care for injured workers while helping clients contain costs and control utilization.

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