

inside

front page news

Trends in Workers' Compensation
Prescription Drug Expenditures

feature articles

Options Sought in Balancing
Painkillers

■ 3

American Heart Association Issues
Statement on NSAID Use

■ 3

Chronic Pain Increases
in America's Workforce

■ 3

Lyrica Approved to
Treat Fibromyalgia

■ 3

regular departments

Clinical Literature
Digest Studies

■ 4

FDA Update

■ 5

FDA MedWatch Reports

■ 5

Trends in Workers' Compensation Prescription Drug Expenditures

There have been several significant new financial and prescribing trends in the workers' compensation market during the last 24 months. The trends identified have been mined from the nation's largest single database of workers' compensation prescription transactions and assembled to provide insight into this difficult-to-manage area of healthcare. Understanding the current pharmaceutical industry and medication financial drivers in the workers' compensation industry is vital in providing insight into future trends. PMSI Clinical Pharmacist, Matthew Foster, PharmD, BCPS, has authored *Identified Trends in Prescription Drug Expenditures in the Workers' Compensation Market 2005–2006*. This report outlines the utilization trends and drivers for the top therapeutic classes in workers' compensation over the last 24 months. Below are some highlights from Dr. Foster's trends paper. To obtain a copy of the full report, please send a request to marketing@pmsionline.com.

TOP PRESCRIBED THERAPEUTIC CLASSES BY PERCENT OF TOTAL MEDICATION EXPENSE

Medication Class	Typical Medications	2006 Industry
Narcotic Analgesics (Opioids)	OxyContin, Percocet, Vicodin, Lortab, etc.	32.5%
Anticonvulsants	Neurontin, Lyrica, Gabitril, etc.	10.7%
Anti-inflammatory (NSAID)	Celebrex, Mobic, Motrin, Voltaren, etc.	10.5%
Muscle Relaxants	Flexeril, Skelaxin, Soma, etc.	9.1%
Antidepressants	Cymbalta, Effexor, Zoloft, Lexapro	8.0%
Dermatologics	Lidoderm	5.3%
GI Medications	Nexium, Prevacid, Pepcid, Zantac	4.4%
Sedatives	Ambien, Lunesta, Restoril	3.8%
Anti-anxiety	Xanax, Ativan, etc.	2.1%
Antipsychotics	Seroquel, Zyprexa, Geodon, etc.	1.6%
Total percent of top 10 medication classes		88%

There has been very little change in the ranking of the Top 10 drug classes over the last two years, mainly due to the large percentage of total expenditures within the Top 3 classes (see above table). Opioid analgesics, NSAIDs, and anticonvulsants are all used in the treatment of pain syndromes. Although the top medication classes have not changed significantly, the individual medications within each of the classes have changed considerably. The Top 5 medication classes alone still account for almost 70% of the total drug expenditures, and the Top 10 account for 88% of all expenditures.

continued on page 2

Narcotic Analgesics

Short-Acting Opioid Analgesics. Although the hydrocodone-APAP and oxycodone-APAP tablets remain the most commonly prescribed short-acting narcotic analgesics, the high cost of oral fentanyl products continues to make the largest financial impact in this category.

Long-Acting Opioid Analgesics. Long-acting opioids will continue as an option in the treatment of chronic pain. The loss of a generic version of OxyContin and the increasing utilization of Opana ER and Ultram ER may result in significantly higher costs in this class.

Anticonvulsants

The use of anticonvulsants will continue to expand within workers' compensation patients as an option in treating "chronic pain. Lyrica and Gabapentin will continue to dominate the medications in this class.

The Top 5 medication classes alone still account for almost 70% of the total drug expenditures, and the Top 10 account for 88% of all expenditures.

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)

The NSAIDs will continue to be used commonly for the treatment of mild-to-moderate pain. There are continuing concerns with the safety of these agents when used for extended periods of time. Although the total costs have been decreasing since 2005, this is expected to level off or begin a steady increase as Celebrex begins advertising to consumers and healthcare practitioners in 2007.

Skeletal Muscle Relaxants

The therapeutic class of muscle relaxants will continue at the current rates of prescribing and total costs.

Antidepressants

Antidepressant use may remain flat with regard to total transactions, but costs may continue to increase due to increases in prescribing of brand name medications such as Cymbalta and Effexor XR.

Dermatologics

Although the use of Lidoderm is continuing to rise only slightly, the total costs will continue to increase due to more frequent administration of the patches and as medication prices rise.

Gastrointestinal Medications—Anti-Ulcer Agents (Antacids)

Because of the high use of NSAIDs acutely and chronically in workers' compensation injuries and the increased awareness to the dangers of GI ulceration, the use of antacids will continue to slowly increase. Total costs have been relatively stable over the last 12 months and should continue to remain stable.

Sedatives

Sedative use should level off in the next year. Expenses will most likely continue to increase despite the availability of a generic formulation of Ambien.

Anti-Anxiety

There are no significant increases in utilization of anti-anxiety agents expected. Costs are expected to level off or continue at a slight decrease.

Antipsychotics

The impact of antipsychotics on total medication expenses remains low; however, it continues to be an important medication class due to its use with injured workers who are primarily outside of the approved medication use.



features

Options Sought in Balancing Painkillers

The U.S. government estimates that 1 in 10 Americans experience pain that persists for a year or longer. For millions of sufferers, the only solution is long-term therapy with opioid pain relievers. An estimated 6 million patients are currently utilizing some form of long-term opioid therapy. Many worry that opioid pain relievers may not be the answer but rather the problem as fears of abuse and addiction continue to flood the media. The truth is that only a small percentage of patients become dependent on this class of medication. Recently, scientists from the National Institutes of Health (NIH) released a statement specifying that most patients who are vulnerable to prescription drug abuse are typically suffering from psychiatric disorders such as depression and anxiety. Closer monitoring may be warranted in this particular patient population. "Opioids are not dangerous if you know how to use them properly," states Dr. Nora Volkow, who presently acts as chief of the NIH's Institute of Drug Abuse. "We need to develop the knowledge that maximizes our ability to use them properly." Scientists are currently searching for new medications that have decreased abuse potential to ensure that pain sufferers obtain the treatment they need while simultaneously attempting to decrease the potential for abuse.

Lyrica Approved to Treat Fibromyalgia

The U.S. Food and Drug Administration approved Lyrica® (pregabalin) as the first medication to treat fibromyalgia. Affecting 3 to 6 million people per year in the U.S., fibromyalgia is a disorder characterized by chronic pain, fatigue, sleep problems, muscle stiffness and tenderness. Approval for this new indication was based on two double-blind, controlled clinical trials, involving approximately 1,800 patients. Doses of 300 to 450 milligrams daily were used, and some patients experienced decreased pain and improved daily functions after taking Lyrica. The exact mechanism by which the medication produces such effects is still unknown. Lyrica, which is manufactured by Pfizer, was initially approved by the FDA in 2004 for the treatment of neuropathic pain caused by diabetes and shingles, and in 2005 for the adjunctive treatment of partial seizures.

American Heart Association Issues Statement on NSAID Use

The use of non-steroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen and naproxen, has long been a popular treatment option for patients experiencing different painful conditions ranging from minor aches and pains to arthritis. Until the pivotal clinical trials that eventually led to the withdrawal of certain COX-2 inhibitors, such as Vioxx, from the market, most clinicians were only aware of a handful of adverse side effects associated with the use of these analgesics. Recently the American Heart Association released its guidance summary on the appropriate use of NSAIDs. The statement warns of an increased risk of cardiovascular events such as heart attacks, strokes and heart failure associated with NSAID use in patients who are already at high risk for these events. The guidelines call for judicious use of this medication class by urging patients and physicians to use the lowest dose and shortest duration of NSAID therapy possible.



Chronic Pain Increases in America's Workforce

A national survey conducted by Ortho McNeil, Inc. and the National Pain Foundation has discovered a 38% increase in the number of employees who report having chronic pain at work over the past 10 years. Although most of those surveyed stated that they would rather not call in sick, 65% of employers reported an increase in lost productivity. These statements indicate the growing trend of 'presenteeism' — known as the decrease in productivity as a result of an employee attending work despite illness or pain. Since the original survey in 1996, increases in chronic pain have occurred despite an increase of 65% in workplace wellness programs. "Persistent chronic pain appears to be increasing in prevalence among U.S. workers as Americans age and lead more sedentary lifestyles," said Rollin Gallagher, MD, MPH, editor-in-chief of the National Pain Foundation web site, and clinical professor and director of the Center for Pain Medicine, Research and Policy at the University of Pennsylvania. "This survey indicates that employees with chronic pain must become their own advocates, understand the impact of their chronic pain and work with their healthcare professional to identify appropriate treatment options."



clinical literature digest studies

STUDY #1: Sumatriptan-Naproxen for acute treatment of migraine: A randomized trial

This set of replicate, randomized, double-blind, single-attack, parallel-group studies were conducted in 118 U.S. clinical centers with a total of 2,956 participants (1,461 participants in the first study and 1,495 participants in the second study) diagnosed as having migraine headaches. Participants were randomized in a 1:1:1:1 fashion to receive a single tablet containing a combination of sumatriptan-naproxen, sumatriptan alone, naproxen alone or placebo. Patients were given a tablet after onset of migraines with moderate-to-severe pain, and recorded perceived efficacy on supplied diary cards. Pain severity was assessed at the following intervals: immediately before dosing; 30 minutes, 1 hour and 1.5 hours after dosing; and hourly from 2 to 24 hours after a dose. Primary outcome measures included headache relief within 2 hours of dosing, absence of photophobia/phonophobia, absence of nausea for the comparison between placebo and combination therapy, and sustained pain-free response for the comparison between combination therapy and each drug individually. Combination therapy with sumatriptan-naproxen resulted in more favorable clinical outcomes than either medication alone, although minor differences in adverse effects (i.e., absence of nausea) were noted between the two studies. The sumatriptan-naproxen single-tablet combination resulted in a similar and well-tolerated adverse effect profile as compared to either monotherapy alone.

Brandes JL et al. "Sumatriptan-Naproxen for Acute Treatment of Migraine: A Randomized Trial." *JAMA*. 2007 Apr 4; 297:1443-54.

STUDY #2: Obesity and workers' compensation: Results from the Duke Health and Safety Surveillance System

Studies have shown that obese individuals have increased mortality and use of health-care services; however, the impact of this effect on workers' compensation has yet to

be determined. This study was aimed at determining the impact of increased body weight as calculated by BMI, or Body Mass Index (defined as weight in kilograms divided by height in meters squared), with the number and types of workers' compensation claims, associated costs, and lost productivity (work days). The study was conducted as a retrospective cohort study and included 11,728 health-care and university employees with at least one health risk appraisal between January 1, 1997 and December 31, 2004. Following data analysis, a clear distinction between BMI and the number and type of claims became apparent. Participants with a BMI ≥ 40 (obesity class III) encountered 11.65 claims per 100 full-time equivalents, while only 5.8 claims were observed in recommended-weight employees. Furthermore, lost work days (183 versus 14 lost work days) and claim costs (\$59,178 versus \$5,396) were lower in the recommended-weight employees. BMI related claims were mainly caused by injuries related to the lower extremity, wrist, hands or back pain or inflammation, sprains or strains, and contusion and bruises. The combination of obesity and high-risk occupation proved to be the most detrimental.

Ostbye et al. "Obesity and Workers' Compensation: Results from the Duke Health and Safety Surveillance System." *Arch Intern Med*. 2007; 167:766-773.

STUDY #3: Long-term use of controlled-release Oxycodone for non-cancer pain: Results from a three-year registry study

This recent study was conducted to evaluate outcomes associated with the utilization of oxycodone controlled-release in the treatment of noncancer pain for a time period of up to three years. Two hundred thirty-three patients were enrolled in this open-label, uncontrolled, prospective, longitudinal investigation and were followed at three-month intervals for up to 36 months. Participants were asked to complete a Brief Pain Inventory (BPI) at each visit, and to rate pain intensity on a 0–10 numeric scale. After baseline observation, patients were also interviewed on a regular basis to observe for the development of adverse effects, drug-related behavior,

or suspicious drug use. Although the study was terminated prior to the three-year goal, decreases in pain were observed by the end of month three, with most patients experiencing an increase in pain relief or no change at all. Adverse effects were minor (constipation and nausea), and most had resolved over the life of the study. Overall, results indicated that oxycodone controlled-release was effective in relieving noncancer pain.

Portenoy RK et al. "Long-term Use of Controlled-Release Oxycodone for Noncancer Pain: Results of a Three-Year Registry Study." *Clin J Pain*. 2007 May; 23(4):287-299.

STUDY #4: Transition from acute to chronic pain and disability: A model including cognitive, affective and trauma factors

Research has suggested that exposure to certain stressors can cause permanent changes to some neurobiological processes. These changes may predispose a person to experience more intense distress and pain following an acute injury. This study was conducted to examine if acute pain severity and disability, baseline depressive symptomatology, and pain beliefs predispose a patient's pain to eventually progress to a chronic state. Participants were recruited from the Sharp Rees-Stealy Acute Back Clinic (ABC) in California and consisted of 84 patients with new onset neck or back pain of less than 8 weeks' duration. Participants were followed for a three-month time period and assessed via questionnaires that addressed pain intensity, pain disability, cumulative trauma exposure, depression, and pain schemas. At the end of the study period, baseline depressive symptoms and pain permanence beliefs were the most predictive in terms of progression to chronic pain. Acute disability was associated with higher baseline depressive symptoms; therefore, indirectly increasing the chances for progression. Baseline pain beliefs and acute pain intensity were not found to be reliably predictive of eventual progression.

Young Casey C et al. "Transition from Acute to Chronic Pain and Disability: A Model including Cognitive, Affective, and Trauma Factors." *Pain*. 2007 May 17. Article in press.

FDA update

New Drug or Formulation

Amrix (cyclobenzaprine HCL extended-release) tablets

Approved: February 2007

Amrix is a long-acting formulation of the skeletal muscle relaxant cyclobenzaprine, which is used as an adjunct to rest and physical therapy for relief of muscle spasms associated with acute, painful musculo-skeletal conditions. Amrix will be available in both 15 mg and 30 mg tablets and should be dosed once daily. Although the administration will be different as compared to cyclobenzaprine regular-release, utilization beyond two to three weeks will still not be recommended.

Flector (diclofenac epolamine) patch

Approved: January 2007

Flector is a patch formulation of the NSAID diclofenac. The patch is intended to provide local analgesia by releasing medication into the skin. Use is indicated for the topical treatment of acute pain due to minor strains, sprains, and contusions. The patch will also carry the black box warning regarding cardiovascular and gastrointestinal adverse effects.

New Indications

Cymbalta (duloxetine), an antidepressant used in the treatment of major depressive disorder, recently gained a new indication for the treatment of generalized anxiety disorder.

Generic Drug Arrivals

Ambien (immediate release), a long-time leader in the non-benzodiazepine sedative hypnotic market, is now available generically as zolpidem tartrate (immediate release).

Coreg, a popular beta blocker medication used in the treatment of high blood pressure as well as moderate-to-severe heart failure, has recently been approved as the generic formulation, carvedilol.

Lotrel, a combination calcium channel blocker/ACE inhibitor medication used for the treatment of high blood pressure, will now be available as the generic equivalent, amlodipine/benazepril.

Norvasc, a popular calcium channel blocker used in the treatment of patients with high blood pressure, is now available generically as amlodipine.

FDA MedWatch Reports

Illegal OxyContin promotion by manufacturer may cause health risks for consumers

Posted May 10, 2007—FDA informed healthcare professionals of criminal charges and civil liabilities brought against Purdue Frederick in connection with several illegal schemes to promote, market and sell OxyContin, a powerful prescription pain reliever that the company produces. The manufacturer's sales force was trained to make false claims about the product to healthcare professionals, thereby, misrepresenting OxyContin by illegally promoting the drug as being less addictive, less subject to abuse, and less likely to cause tolerance and withdrawal than other pain medications. These practices falsely promote the product and may cause health risks for consumers.

Ambien (zolpidem tartrate)

Posted March 14, 2007—FDA notified healthcare professionals of its request that all manufacturers of sedative-hypnotic drug products, a class of drugs used to induce and/or maintain sleep, strengthen their product labeling to include stronger language concerning potential risks. These risks include severe allergic reactions and complex sleep-related behaviors, which may include sleep-driving.

Sleep-driving is defined as driving while not fully awake after ingestion of a sedative-hypnotic product, with no memory of the event. FDA also requested that each product manufacturer send letters to healthcare providers to notify them about the new warnings, and that they develop Patient Medication Guides for the products to inform consumers about risks and advise them of potential precautions that can be taken.

Zanaflex (tizanidine)

Posted April 11, 2007—Acorda Therapeutics and FDA informed healthcare professionals of changes to the *Contraindications* and *Warnings* sections of the product labeling for Zanaflex, a drug used to treat spasticity. In pharmacokinetic studies where tizanidine was co-administered with fluvoxamine or ciprofloxacin (CYP1A2 inhibitors), the serum concentration of tizanidine was significantly increased and potentiated its hypotensive and sedative effects. Although there are no clinical studies evaluating the effects of other CYP1A2 inhibitors on tizanidine, co-administration of tizanidine with other CYP1A2 inhibitors (zileuton, other fluoroquinolones, antiarrhythmics, cimetidine, famotidine, oral contraceptives, acyclovir and ticlopidine) should be avoided.

Antidepressant black box warning expansion

Posted May 2, 2007—FDA notified healthcare professionals that the Agency proposed that makers of all antidepressant medications update the existing black box warning on the prescribing information for their products to include warnings about the increased risks of suicidal thinking and behavior in young adults ages 18 to 24 years old during the first one to two months of treatment. The proposed labeling changes also state that scientific data did not show this increased risk in adults older than 24 years of age and that adults 65 years of age and older taking antidepressants have a decreased risk of suicidality. The proposed updates apply to the entire category of antidepressants. Individuals currently taking prescribed antidepressant medications should not stop taking them and should notify their healthcare professional if they have concerns. Manufacturers of antidepressant medications will have 30 days to submit their revised product labeling and revised Medication Guides to FDA for review.

continued on page 6

FDA MedWatch Reports

continued from page 5

Online prescriptions

Posted February 16, 2007—FDA informed consumers and healthcare professionals regarding the possible dangers of buying prescription medications online. Individuals who ordered Ambien, Xanax, Lexapro and Ativan over the Internet received a product that contained haloperidol, a powerful antipsychotic drug. Several consumers experienced difficulty in breathing, muscle spasms and muscle stiffness after ingesting the suspect product and had to seek emergency medical treatment. Haloperidol can cause muscle stiffness, spasms, agitation and sedation. Taking medication that contains an active ingredient other than what is prescribed by qualified healthcare professionals is generally unsafe. FDA urges consumers to review the FDA web site for additional information prior to making purchases of medications over the Internet.

PMSI—The Only Solution You Need.

PMSI is the single-source solution for workers' compensation. Founded in 1976, today PMSI is the nation's largest full-service network provider of pharmacy, Medicare Set-Asides, medical services and equipment, and clinical services. PMSI promotes quality care for injured workers while helping clients contain costs and control utilization. PMSI is a subsidiary of AmerisourceBergen Corporation—a Top 50 company in the Fortune 500 list and among the Top 5 in the Pharmaceutical Service Providers category.



Single-Source Solution
for Workers' Compensation

tmesys®

msa
Formerly Health Advocates Inc.
and HAI West

medical services
and equipment

clinical

pharmacy

Editors: Nelson Aragon, PharmD,
Melissa Ray, PharmD

© 2007 PMSI. All rights reserved.
Arkos is a trademark of PMSI, Inc.
and Oxycontin is a registered
trademark of Purdue Pharma L.P.
C1067-0707-01

175 Kelsey Lane
Tampa, FL 33619

PH: 877.ASK.PMSI

www.pmsionline.com