2014

WORKERS' COMPENSATION DRUG TREND REPORT

Progressive Medical & pmsi

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METHODOLOGY

The 2014 Drug Trend Report is based on paid workers' compensation transactions covering the 2012–2013 time periods. More than 300,000 claims and in excess of six-million prescriptions were analyzed. The report includes in-network prescriptions captured through the application of our network enforcement solutions. It excludes clients who have had less than two years' history with our company.

Data from Progressive Medical and PMSI has been merged into a single data set and analyzed as one unit. In circumstances where legacy methodologies were different, we compared the two to establish the go-forward approach for the combined organization.

> “Our business is not just about transactions or line items processed. It’s about ensuring injured workers receive exactly what they need when they need it, and delivering value to our clients.”

OVERALL COST AND UTILIZATION TRENDS

During 2013, Progressive Medical and PMSI achieved an overall decrease in the average prescription cost per claim of 1.7%. This decrease was driven by changes in medication utilization, as evidenced by the 6.3% decrease in average cost per days’ supply per claim in conjunction with a 3.2% reduction in product and claim mix. This more than offset growth in prescription medication inflation of 7.8%.

As for how we accomplished this, there was not one single tactic, effort, or approach that achieved this result. No one particular product or service caused a claim to pivot away from misuse or abuse. Nor was there an individual legislative amendment or rule change solely responsible for drastic reform. Rather, our success is directly attributed to the integration of strong network enforcement programs, advanced analytics, holistic utilization management, and collaborative clinical interactions executed through a series of deliberate, well-timed, and persistent actions by a team of experienced professionals. Leveraging proprietary connectivity and technologically advanced communication portals, we provide our clients with the data, tools, and insight needed to make the right decisions so that the injured workers we serve receive the right medication at the right time.

Figure 1 - Top 25 Medications as a Percentage of Total Spend with AWP, page 49
Figure 2 - Top 25 Medications by Percentage of Total Rx with AWP, page 50
Figure 3 - Top 25 Medications Ranked by Daily Spend, page 51

↑7.8%
Average Wholesale Price

↓6.3%
Average Cost per Days’ Supply

↓3.2%
Product and Claim Mix

↓1.7%
Average Prescription Cost per Claim

“Effective cost management is heavily reliant on the ability to mitigate the influence of out-of-network bills, and both compounded and specialty medications, at every stage of the claim.”

COST MANAGEMENT

Average Wholesale Price (AWP)

Prescription drug inflation in AWP continues to follow an upward trend, growing by 7.8% this year. For brand medications, the percentage increase of AWP inflation averaged 13.3%, whereas the percentage of AWP inflation for generic medications increased by 0.7%.

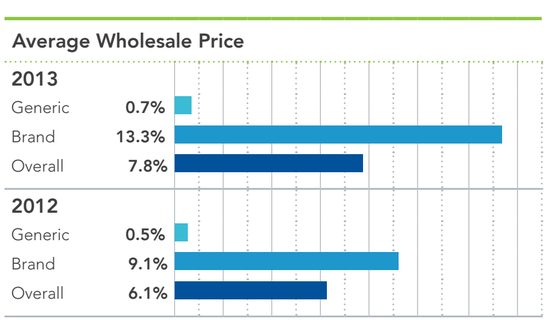
Analysis shows that the AWP for many top brand medications grew at a rate of approximately 20%, including Celebrex®, Cymbalta®, and Lyrica®. Brand formulation Percocet® grew by 24% this year, consistent with its pattern of regular increases in AWP since its release on the market. Other brand medications whose price grew over 20% include Exalgo® (23%), Fentora® (21%), and Amrix® (54%). It appears pricing for Exalgo may be following the trend of other medications that have had a substantial increase in the AWP prior to the release of a generic alternative. Also contributing to the 13.3% inflation in brand AWP are new medications that entered the market; for example Khedezla® a serotonin-norepinephrine reuptake inhibitor (SNRI) and Zubsolv® (used for opioid dependence).

With respect to generic medications, in 2013 the inflation rate of 0.7% is higher than reported in our previous drug trend reports. Comprising the highest percentage of our overall generic drug spend, hydrocodone/APAP (the direct generic alternative for brand name Vicodin® and Norco®), had an inflation rate of 6%. The therapeutic class of muscle relaxants also had meaningful inflation in AWP. An example of this is metaxalone (the generic for Skelaxin®), which grew at 7%.

Figure 4 - AWP Inflation -Top 25 Brand Medications, page 52
Figure 5- AWP Inflation -Top 25 Generic Medications, page 52

As this document goes to press, additional medications continue to show increases over prior years. For example, the direct generic alternative for brand name Percocet® and Endocet®, oxycodone-acetaminophen 5 mg-325 mg has increased by 220.7%, oxycodone-acetaminophen 7.5 mg-325 mg by 87.5% and oxycodone-acetaminophen 10 mg-325 mg by 94.6%. Growth in prices for these products may be traced to the Food and Drug Administration (FDA) initiative to limit the amount of acetaminophen to 325 mg per dosage unit in opioid combination products by 2014. Another potential reason for these price increases may be the country's push to decrease the use of opioid analgesics, yielding to economic supply and demand forces. Others have also postulated such increases are due to the changes in health care law and the uncertainties associated therewith.

Regardless of the cause, the continued development in AWP inflation for both brand and generic medications is largely beyond the payer's control. The ability to effectively mitigate the influence of out-of-network bills and both compounded and specialty medications is one way payers may experience cost savings. A proactive mail order program may also serve to lower costs.



Network Enforcement

One of the keys to successful cost containment (and utilization management) is a Pharmacy Benefit Manager's (PBM) prowess at driving transactions "in-network," whether they are filled at the retail pharmacy or via a non-traditional source such as a physician's office or clinic. Not only are out-of-network prescriptions more costly on a per transaction basis (the price differential between an in-network prescription and an out-of-network prescription has increased from 14% in 2012 to 22% in 2013), but they also carry a higher administration cost, are inherently inefficient, and can impede a payer's ability to completely understand the injured worker's medication therapy regimen.

Retail Network Penetration and Third Party Billers

We have combined the best aspects of third party billing, bill review, and pharmacy benefit management into one comprehensive solution. Using an integrated and proprietary technology platform, we electronically adjudicate claims with every national pharmacy chain, as well as virtually all independent pharmacies, in real time. By utilizing a common eligibility file we efficiently and accurately manage transactions at the pharmacy point of sale, resulting in retail network penetration rates of up to 98%.

This unique solution is invaluable to our clients for a variety of reasons — the most obvious being cost savings as network discounts are applied to nearly all retail prescriptions at the point of sale. Capturing more prescriptions "in-network" also has a positive influence on utilization, providing valuable data that fuels our statistical models and analytics and guides clinical decision-making (discussed later in this report). Payers also benefit from administrative cost savings and efficiencies.

Specialty Network and Physician Dispensing

A growing number of medications are being dispensed by physicians. As such, the PBM's ability to establish contractual relationships with these non-traditional dispensers is important to achieve optimal cost control. Our Specialty Network continued to expand in 2013; as a result, our clients recognized cost savings as prescriptions dispensed by physicians, and other non-traditional sources, were brought within the purview of our program.

In 2013, spend related to physician-dispensed medications in our Specialty Network decreased by 14%. As a percentage of overall spend, the cost of physician-dispensed medications was flat. The top six states in which physician-dispensed medications were prevalent included California, Florida, Illinois, Louisiana, Maryland, and Pennsylvania.

The Benefits of Integrated Network Enforcement

- Paper bills virtually cease.
- Network discounts are applied to more prescriptions, resulting in greater cost savings.
- Formulary controls, drug utilization review edits, and program business rules are consistently applied, starting with the first fill.
- Collection, eligibility, and verification calls are practically eliminated.
- More data is captured, allowing payers to more proactively manage the injured worker's medication therapy regimen.
- Payers are better equipped to spot the warning signs of misuse or abuse so that when necessary, intervention may occur earlier in the claim.
- Therapy duplications, drug interactions, refill patterns, patient adherence, and other therapeutic concerns are identified sooner, allowing for more informed and empowered medication management.

Mail Order

Effective mail order programs are an important component of overall pharmacy cost management because of the lower prescription costs associated with those programs. Catastrophic claims, as well as those where medication therapy has stabilized or otherwise involve long-term medication needs are long recognized as viable candidates for prescription management using mail order. In addition, mail order programs offer convenience to the injured worker and their caregiver. In 2013, for every 10% shift in days' supply from retail to mail order, our clients experienced a 1.2% reduction in spend without any increase in administration cost or effort on their part.

As would be expected, the days' supply for a mail order prescription is higher than its retail equivalent, at 53.5 days and 24.6 days, respectively. Similarly, the average cost per days' supply of mail order prescriptions was 17.3% less at $4.83, versus $5.84 for its retail equivalent.

> "....the average cost per days' supply of mail order prescriptions was **17.3% less** than its retail equivalent..."

Compounded Medications

Throughout 2013 there were numerous recalls and withdrawals of compounded medications in injectable formulations for a variety of reasons, including lack of sterility, product contaminants (suspect particles), and mislabeled product ingredients. While some of these issues are more clinically significant than others, the vast majority of these recalls did not impact our clients because the injectable products involved were not being utilized by injured workers in our book of business. Topical compounded medications are more common in workers' compensation.

On average, there are four to five individual ingredients in the compounded medications we reviewed through our program. A listing of some of the more commonly encountered ingredients is found in Appendix, Figure 6. Each ingredient is evaluated against our injury-specific formularies and Medication Plans, and requires prior approval. This process ensures an informed decision on the part of the claims professional. It also provides an opportunity to weigh the appropriateness of the compounded medication, which in turn, helps keep costs down, as compounded medications are often more expensive than first-line therapy options.

In 2013, compounded medications represented 0.69% of the total number of prescriptions, up from last year when the count represented 0.62% of the total. As evidenced by the change in daily spend (also shown in Appendix, Figure 6) for the top 10 ingredients found in compounded medications, the average billed amount for compounded medications is also increasing. This emphasizes the importance of proactive efforts, such as those deployed through our programs, to effectively manage their cost.

Figure 6 - Top 10 Ingredients Found in Compounded Medications, page 53

Specialty Medications

Specialty medications are those used to treat complex medical conditions including, but not limited to, rheumatoid arthritis (RA), Hepatitis C, human immunodeficiency virus (HIV), some cancers, and certain blood clotting disorders. These conditions are more commonly encountered on the commercial or group health side of health care. This is not to say that specialty medications are not encountered in workers' compensation; it's just not nearly as common an occurrence. This is because the risk of exposure is generally restricted to either certain occupations, such as emergency responders or health care practitioners, where exposure to blood or other body fluids that carry infectious diseases is high, or as the result of a comorbid condition that has been exacerbated by the presence of a workers' compensation injury. Specialty medications did not represent significance to our book of business from the standpoint of either cost or utilization.

Specialty medications are receiving a good deal of attention in both the group health and the workers' compensation pharmacy arena for two primary reasons — quest for innovation and cost. The pharmaceutical industry is actively searching for new chemical entities and as a result, there are many new medications in the pipeline. For the most part, these new medications will not be encountered in workers' compensation except in very precise circumstances (i.e., a needle stick claim), or if determined compensable secondary to the initial injury (i.e., the use of blood-thinning injectable medications post-surgery). When they are, however, they are extremely expensive medications. Some examples are highlighted in Appendix, Figure 7.

Our programs are deliberately constructed to comprehensively manage specialty medications at every stage of the claim. When specialty medications are deemed appropriate for the claim, the injured worker's compliance with the medication therapy should be closely monitored through file resolution to assure the treatment being paid for is adhered to.

Figure 7 - Specialty Medications, page 54

> "....this is not to say that specialty medications are not encountered in workers' compensation; it's just not nearly as common an occurrence... **Specialty medications did not represent significance to our book of business** from the standpoint of either cost or utilization."

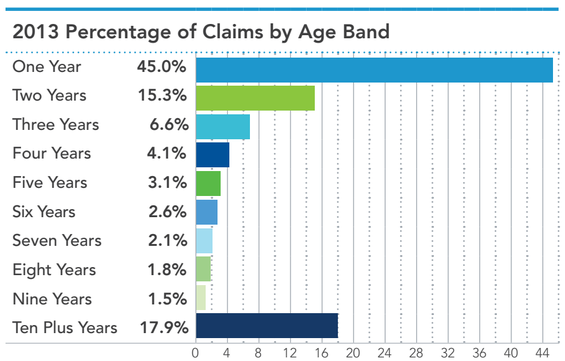
“Our programs are driven by evidence-based medicine, both national and regional approved medical guidelines, and guided by experienced clinicians. By working collaboratively with our clients and other industry stakeholders, we are achieving better outcomes.”

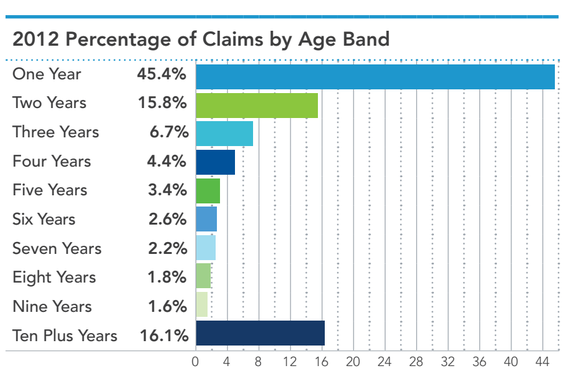
UTILIZATION MANAGEMENT

Claim Age

One of the primary drivers of utilization is the age of the claim. Generally speaking, as the duration of an injury increases, the average cost per prescription also increases. This is typically due to higher utilization of brand medications later in the claim or because of failure of first line or generically available medications used to treat the injury. In addition to the higher cost per prescription, the average number of prescriptions per injured worker also rises with increased claim duration.

The claim age profile of our book of business increased slightly from 2012 to 2013. Specifically, the number of claims 10 years or older moved from 16.1% to 17.9% of our total book of business; meanwhile claim age decreased in all other age bands. Although we would have expected the aging of our book to result in an increase in cost per claim, this was not the case. Both utilization and prescription cost per claim decreased in all claims, regardless of the age of claim.





Opioid Analgesics and Morphine Equivalent Dose (MED)

Opioid Analgesics

IMS Health recently reported the number of prescriptions written for opioid medications went down for the second year in a row; moving from 241 million to 232 million[1]. Although this is a trend that Progressive Medical and PMSI also saw, there is more to the story than just the number of prescriptions. The quantity of medication per prescription and the days' supply are factors that must also be considered.

In 2013, 62.1% of injured workers using prescription medications used opioid analgesics. This is down from 64.2% — a positive shift. There was also a 5% reduction in the utilization of opioid analgesics and the prescription cost per claim decreased by 6%. Moreover, those who used opioid analgesics used lower doses than the previously reported year. MED declined by 9.6%, a significant year-over-year reduction in MED per claim.

↓5.0%
Opioid Utilization

↓6.0%
Prescription Cost per Claim

↓9.6%
MED per Claim

The percentage of injured workers using prescription medications who used opioid analgesics decreased to **62.1%**

Morphine Equivalent Dose

There are different types of opioid analgesic medications that range in potency. To effectively compare different opioids to each other, opioids should be converted to a standard potency. This is done by using morphine as the "gold standard" for opioid medications; MED is the dose of the opioid medication as if it were morphine. For example, if a patient is taking OxyContin® 30 mg twice daily (60 mg total daily dose), this would convert to an approximate morphine equivalent dose of 90 mg or 90 mg MED daily since OxyContin is more potent than morphine. However, if a patient were taking codeine 30 mg four times daily (120 mg total daily dose), this would equate to approximately 18 mg MED daily because codeine is less potent than morphine[2].

While consensus among prescribers regarding what is the safest, most therapeutically effective MED per day has been hard to achieve, it is generally agreed that a collaborative approach involving education, effective screening of patients, and careful monitoring of the response to treatment is beneficial. Risk Evaluation and Mitigation Strategies (REMS) is one such educational process that has helped prescriber and patient alike learn more about long-acting opioid analgesic medications in recent years. Use of screening tools such as the Opioid Risk Tool (ORT) helps identify whether the patient may have a propensity for misuse or abuse. And, by closely monitoring the patient's pain scores, Activities of Daily Living (ADL), and overall functional improvement, a physician is better positioned to intervene earlier should a safety concern be identified or it be determined that the patient is not otherwise responding to the opioid therapy regimen.

Progressive Medical and PMSI is well-versed in the management of opioid analgesics for the treatment of acute and chronic pain. Our programs are driven by evidence-based medicine, both national – and regional – approved medical guidelines, and guided by experienced clinicians. By working collaboratively with our clients and other industry stakeholders to implement our program, we are effectively bending the curve away from high-cost misuse and abuse situations and towards better outcomes.

ACOEM Updates Medical Treatment Guidelines

In March 2014, the American College of Occupational and Environmental Medicine (ACOEM)[3] released an updated medical treatment guideline suggesting MED doses should be limited to 50 mg in most cases, particularly in the acute setting, although sub-acute and chronic pain patients may require higher doses. Previously, ACOEM recommended vigilance at doses above 120 mg MED irrespective of duration of therapy. The new guideline also stated short-acting, breakthrough pain opioid analgesics are generally not recommended in chronic pain. Long-acting baseline pain agents should be utilized in this patient population, if necessary. Previously, ACOEM guidelines were less specific. The release of these guidelines represents the continuation of a long line of efforts aimed at curbing the inappropriate prescribing of opioid analgesics in the workers' compensation patient population. As we release this report, our Pharmacy Oversight Committee is reviewing the new guidelines to determine their influence, if any, on our program. Future guidance on this subject will be forthcoming.

Generic Efficiency and Generic Utilization

In 2013, generic efficiency remained strong, at 99.7%. This high rate of generic efficiency is reflective of our effective point-of-sale and formulary controls that require generic fulfillment unless otherwise dictated by the state of jurisdiction or the prescriber's requirement that the medication be dispensed as written.

In addition to high, stable levels of generic efficiency, generic utilization improved 1.9 points in 2013, moving from 74.1% to 76.0%. One of the reasons for this increase is the application of our Generic Opportunity Service, wherein we reach out to the prescriber, claims professional, or injured worker (where allowable) via written correspondence to discuss the availability of therapeutically equivalent, generic medications. To gauge the impact of this program, we looked at 5,044 drug-level interventions performed over a 12-month period of time. In doing so we found that as a result of our outreach, clients realized additional cost savings of $1.5 million.

Looking forward, we anticipate the following medications will have a generic release with the potential to reduce medication spend for our clients: Nexium®, Naprelan®, Abilify®, Zyvox®, Axert®, and Celebrex®.

Figure 8 - Top 25 Generic Medications including Generic Efficiency, page 54

"One of the reasons for this increase is the application of our Generic Opportunity Service.... as a result of our outreach clients realized additional savings of $1.5 million."

In 2013 generic efficiency remained strong at

99.7%

“We use predictive analytics to leverage our expansive repository of data and veteran expertise in workers’ compensation pharmacy to predict which claims will result in long-term pharmacy cost... these predictions allow for smarter clinical triage and drive better decision making.”

ANALYTICS, INTERVENTIONS, AND CLINICAL INTERACTIONS

Progressive Medical and PMSI use predictive analytics to leverage our veteran expertise in workers' compensation pharmacy and expansive repository of clinical data (the largest in the industry) to predict which claims will result in long-term pharmacy costs. Specifically, we use multi-variate, log-linear regression models to predict pharmacy costs for each individual injured worker. These models use data such as the injured worker's age, geography, prescriber, medications filled, and local demographics to identify the claims that will have the highest pharmacy costs in the future. These predictions allow for smarter clinical triage and drive better decision making, relative to where we focus our resources (and those of our clients) to help protect their financial interests while optimizing therapy and advancing recovery for the injured worker.

Early Intervention

The process begins once a claim has reached 120 days post injury. At this point, enough data has been collected on the claim that we can begin using predictive analytics. After ranking claims based on their highest expected cost, our clinical team examines the most extreme cases and determines what can be done to positively influence the outcome of the claim.

By intervening on just 10% of injured workers four months after injury, our models identify 67% of the claims that will be long-term pharmacy cost claims. This means our models are accurately identifying the claims that require attention, we are able to generate better outcomes — both clinically and financially.

We continue to see positive results from our predictive models. We measured the risk of more than 23,000 claims in our early intervention program. The goal of this program is to find the needles in the haystack: the less than 10% of claims that make up 90% of long-term pharmacy costs. After predicting the long-term costs of these 23,000 injured workers, our clinical team examined 355 of them and intervened on 138 high-risk claims. We measured the cost of these claims before and after intervention and calculated the corresponding return on investment (ROI). The result was a favorable annual ROI for each claim of 5:1.

> "...**our models** are accurately identifying the claims that require attention, we are able to **generate better outcomes** — both clinically and financially."

Long-term Intervention

Once a claim has reached 180 days, our interventions shift in focus, targeting changes in behavior to any chronic issues that have started to develop. Often, these long-term claims require an in-depth Peer-to-Peer conversation with the prescribing physician to facilitate a change to the injured worker's medication therapy regimen.

Recently, retrospective studies analyzed the impact of our Peer-to-Peer interventions. This study included 267 injured workers representing a total of 893 reviewed medications from various therapeutic classes. Overall, this service achieved a 62% success rate in eliciting a change to an injured worker's therapeutic regimen, resulting in a realized savings of $3,259.09 per case. When compared to the initial cost of the review, our clients realized an overall 4:1 return on investment when contact was established with the injured worker's prescriber (contact was established for 79% of the cases).

When contact was not established between the peer physician and prescriber, the actualized savings and success rate were not as robust. This is however, not to say these cases were devoid of savings. In fact, a sentinel affect was observed; even though the prescriber would not participate in the outreach, therapy changes and cost savings were noted. In addition to the beneficial changes in medication utilization and total spend, we also found an overall decrease in high-risk therapy associated with ongoing medication use. Peer-to-Peer outreach did not just result in a shift to less expensive therapy; it resolved therapeutic concerns.

> "**Peer-to-Peer outreach** did not just result in a shift to less expensive therapy; it **resolved therapeutic concerns.**"

Clinical Interactions

While the use of advanced analytics undoubtedly bolsters the efficacy of our programs by facilitating earlier, more informed clinical triage, we are not solely reliant upon analytics to guide us at every step of the claim. Our highly-trained team of clinicians (including both nurses and pharmacists) is well versed in workers' compensation and medication therapy management. Their veteran expertise is applied to claims at every stage to help our clients address the various factors that influence outcomes.

Multiple Prescriber Service

The use of multiple prescribers can cloud visibility into the injured worker's medication therapy regimen and could result in safety concerns as potential drug interaction, therapeutic duplications, adverse side effects, and potential misuse and abuse situations are not communicated to all involved. These concerns are heightened when the medication therapy involves opioid analgesics; in fact, current guidelines suggest utilization of a single prescriber (or lead prescriber if multiple prescribers are warranted for the claim).

Every month we identify injured workers who have received prescriptions for opioid analgesics from more than one prescriber. We then send a letter to each identified prescriber to make them aware that there are multiple prescribers treating the injured worker and offer guidance on any identified therapeutic concerns.

Over a 12–month study period, 12,974 injured workers were identified as having received a multiple prescriber intervention. In response to our outreach, 94% of injured workers converted to a single prescriber, which contributed to a 9.6% decrease in total spend for the study group.

Urine Drug Testing & Monitoring (UDT&M)

Integrated within our pharmacy program, UDT&M has been found to be a useful compliance tool, helping payers and physicians confirm the injured worker is adhering to their medication therapy regimen. Such testing is also helpful in identifying possible fraud, diversion, and misuse or abuse situations.

Candidates for UDT&M are identified by our clinical services team using a proprietary application. We then engage with the testing laboratory and the prescriber; the testing is completed and the results analyzed. Where indicated, additional clinical guidance and oversight is provided. Similar to our other clinical programs and intervention tools, the goal is to positively influence the injured worker's therapy regimen by making certain they are receiving the right medication at the right time.

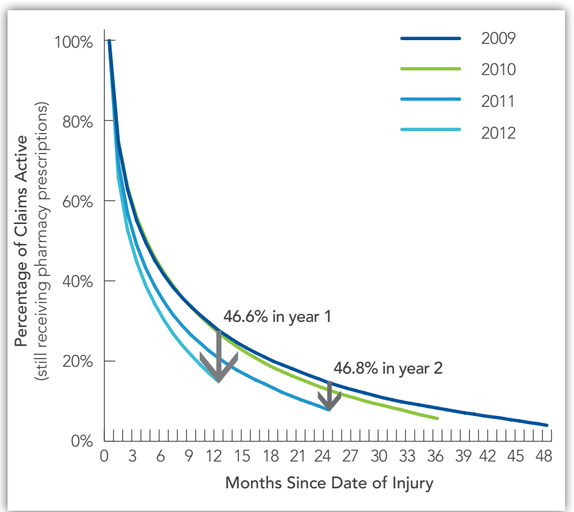
> "Our highly trained team of clinicians (including both nurses and pharmacists) is well versed in workers' compensation and medication therapy management; their veteran expertise is applied to claims at every stage to help our clients address the various factors that influence outcomes."

We completed a comprehensive study to assess the benefits and cost savings of our UDT&M service. The study showed a decrease in all measures of utilization, including a 32% reduction in utilization of opioid analgesics and a 26% reduction in total utilization of all medications, regardless of drug class.

By providing prescribers with additional information regarding unexpected drug test results, including detailed information regarding possible explanations for the results, the UDT&M service has successfully driven down the utilization of high-risk medications. In addition, injured workers enrolled in the UDT&M service saw a reduction in medication misuse risk factors. For further details on the study, the poster is available to view online at http://bit.ly/UDMPoster.

Claim Duration of Pharmacy Use

Clients who implement our programs are experiencing shorter claim duration of pharmacy, meaning fewer claims use prescription medications years after the injury. For example, one of our national carrier clients recognized a 46.8% decrease in the likelihood that a claim will mature beyond two years.



This is impactful as fewer active claims have been found to influence a number of payer metrics, including loss ratio (LR) and combined operating ratio (COR); not to mention the influence on adjustor case loads and claim closure ratios. At the employer level, fewer active claims can equate to greater productivity and may lead to lower experience modifications and premium reductions.

> Shared expertise, aligned objectives, and proactive management at every stage of the claim is important to achieving better outcomes.

INDUSTRY INFLUENCES

In addition to cost containment and utilization management, there are a myriad of influences that add complexity to medication therapy management. Unmanaged, the industry influences discussed herein can negatively impact claim outcomes through delayed return to work, higher costs, higher Medicare set-aside allocations, or worse — dependency, misuse, and abuse. Through shared expertise and aligned objectives, clients of Progressive Medical and PMSI are well-equipped to address these influences holistically at every stage of the claim.

Aging Population

Clinical research suggests that chronological age may play an important role in the types of workplace injuries observed and the progression of such injuries to more chronic conditions[4]. The natural aging process is one reason. Body functions begin to decrease as early as the third decade of life.

Advanced age is typically associated with a higher incidence of pain (i.e., age-related body deterioration), prolonged recovery, and more prevalent psychiatric factors, such as depression, anxiety, and insomnia. Although these factors are typically not directly related to the workplace environment, their presence may compound an otherwise minimal injury. A recent clinical trial published in the American Journal of Public Health suggests that older Americans are becoming more disabled over time[5].

Drug-to-drug interactions, intensified side effects, and comorbid conditions are all important aspects of medication therapy that should be managed to help curb medication-related complications in the older American. Several medications, as noted in resources such as the Beers list, highlight some of the medications and age-related problems that should be addressed in the aging injured worker. Common to many pain management cases is the use of certain antidepressants as an adjunctive medication. In the elderly patient however, care must be taken to ensure a safe outcome when combined with pain medications or other central nervous system depressants that may intensify cognitive impairment.

Comorbid Conditions

When the treatment of a compensable injury is complicated by a comorbid condition, the overall cost of the claim may escalate. This is because the presence of a cormorbid condition may extend the duration of treatment of the primary injury or become a compensable condition. Proactive management of these influences at every stage of the claim is therefore important to achieve better outcomes. Three of the more commonly encountered comorbid conditions are discussed below.

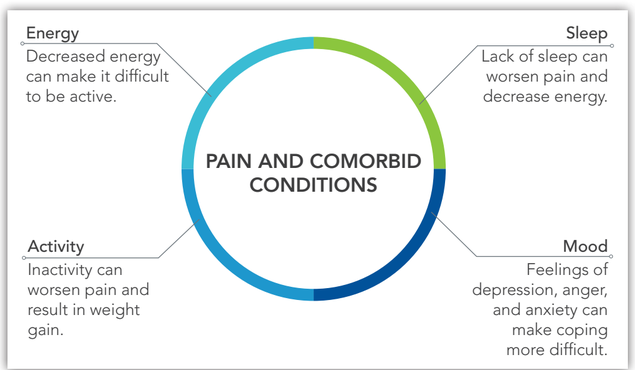
Depression

In workers' compensation, depression is one of the more common and disabling comorbid conditions[6,7]. There is occasionally overlap in causation where depression intensifies the pain sensation leading to reduced mobility. Patients may find themselves relying on their pain medications to enhance their mood, such as through the euphoric response provided by opioid analgesics. Unfortunately, opioid analgesics can further potentiate depressed feelings as a result of their frequent and well-known side effects, including but not limited to fatigue, nausea, and decreased libido.

Since depression usually has a multi-factorial origin, the key strategies to its successful treatment are early identification, eliminating or minimizing the effects of contributing factors, and establishing a multifaceted treatment program consisting of behavioral therapy and pharmacologic management. If underlying depression is not identified early and treated effectively, adequate pain relief can be hindered.

Insomnia

Most of us encounter periods of poor sleep from time to time. Social obligations, entertainment, household and job responsibilities – the many activities of daily living can impede one's ability to obtain the recommended seven to nine hours of nightly rest. Family, friends, work and other circumstances can cause stress that keeps one awake. The existence of an ache or pain is yet another factor that can make it difficult to fall asleep or cause frequent wakening throughout the night. These disturbances can lead to total loss of sleep time or fractured sleep, which prevents the body's obtainment of restorative sleep. One strategy is to ensure that the therapy regimen, both pharmacologic and non-pharmacological, accurately treats the underlying condition.



A review of our transactional data from 2013 suggests that the use of sedatives and hypnotics is experiencing a downward trend, as the therapeutic class fell to the number eight position based on total spend.

Obesity

In workers' compensation, obesity is typically associated with a higher incidence of pain, prolonged healing rates, increased depression, and anxiety. Data from the Duke Health and Safety Surveillance System indicates that obesity may increase a worker's predisposition for injury as compared to their non-obese counterparts, as well as negatively impact lost workdays, medical claims costs, and indemnity claims[8].

Weight gain is a documented side effect of certain prescription medications. Increased weight can become a comorbid condition, resulting in the above mentioned complications, and increased time away from work.

Figure 9 Medications with Weight Gain Potential, page 55

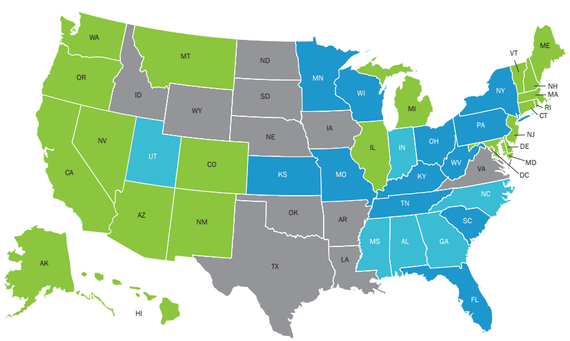
Medical Marijuana

The legalization of marijuana in multiple states across the country for medical and recreational use is generating conversation among all levels of stakeholders in the workers' compensation industry. The complexities of such discussions require careful review of the current knowledge and evidence from trusted sources, particularly with respect to the safety concerns and perceived effectiveness of marijuana when used for medical purposes.

Since 1970, marijuana has been classified as a Schedule I substance, defined by the United States Drug Enforcement Administration (DEA) as having "no currently accepted medical use and a high potential for abuse[9]." Schedule I drugs are considered by the DEA to be the most dangerous drugs with "potentially severe psychological or physical dependence." Other substances sharing the Schedule I classification include heroin, LSD, and ecstasy. As a Schedule I drug, marijuana cannot be processed by pharmacy benefit managers or electronically adjudicated through current standards available in the pharmacy industry. Furthermore, quality control and grading standards have not been implemented to systematically verify the safety and potency of marijuana. This results in a significant barrier to safe prescribing and dispensing processes under our current workers' compensation system.

The potency of marijuana is measured by the percentage of delta-9-tetrahydrocannabinol (THC), the primary psychoactive constituent of marijuana that makes up the sample. According to the American Lung Association[10], THC levels in marijuana had previously averaged 2.3% but have gradually increased to levels higher than 8%, with medical marijuana reaching up to 35%. Marijuana also contains 33 known cancer-causing chemicals (carcinogens) and can deposit four times as much tar in the lungs when compared to tobacco use. With respect to airflow obstruction, one joint of marijuana has been found to be comparable to 2 ½ to 5 tobacco cigarettes, likely caused by inflammation and considered to be "of major public health significance" by the authors of the one study .

Based on the best available scientific evidence and recommendations at this time, in addition to the lack of essential quality control measures, an unchanged Schedule I classification, and the absence of an NDC needed for adjudication and processing, the position of Progressive Medical and PMSI is that medical marijuana will remain excluded from our formularies and Medication Plans. We continue to work closely with all of our stakeholders, sharing our expertise in medication optimization and non-pharmacologic treatment options, to help our claimants reach their maximum level of pain control, function, and opportunity for a successful and safe return to work.



Legalized Medical Marijuana
Legislation pending to legalize marijuana for medical use
Pro-medical use legislation, short of legalization
Medical use of marijuana is prohibited; no pending legislation

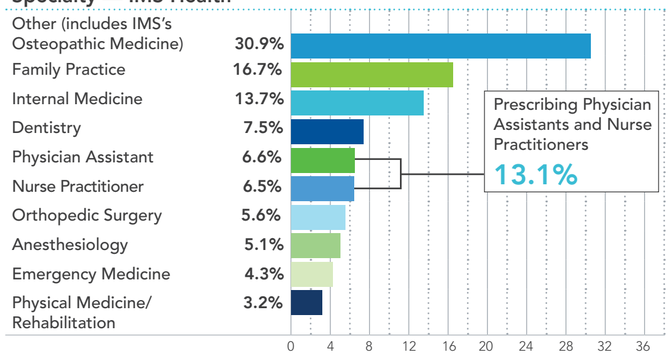
Current as of April 21, 2014; Source: ProCon.org[11]

Prescribing Practices

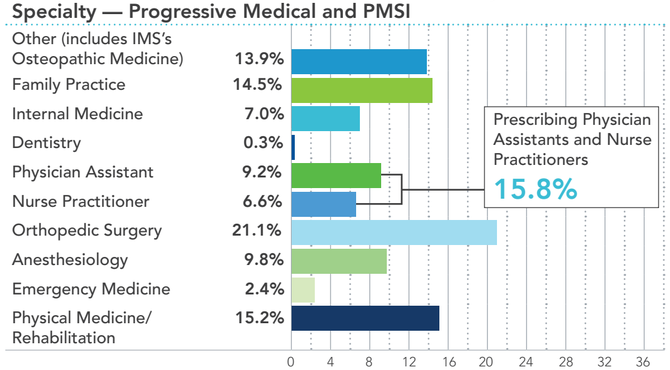
A growing trend in workers' compensation is the increasing number of prescriptions for opioid analgesics being written by Nurse Practitioners and Physician Assistants. As reported by IMS Health, this is also a trend in group health[12]. However, based on our data, the practice appears to be more pronounced in workers' compensation. IMS Health reports just 13.1% of prescriptions written by Nurse Practitioners and Physician Assistants outside of workers' compensation whereas our workers' compensation clients see an aggregate of 15.8% of prescriptions for opioid analgesics written by Nurse Practitioners and Physician Assistants.

All else equal, we found that claims with prescriptions written by Nurse Practitioners have an 8% higher long-term pharmacy cost than those written by other prescribers.

2013 Percentage of Opioid Prescriptions Written by Medical Specialty — IMS Health



2013 Percentage of Opioid Prescriptions Written by Medical Specialty — Progressive Medical and PMSI



GOVERNMENT AFFAIRS

“Over the course of 2013 there was considerable activity on issues that significantly influence cost, utilization, and timely delivery of care...our government affairs team was an active participant in these activities...and an advocate for positive change.”

Over the course of 2013 there was considerable activity on issues that significantly influence the cost, utilization, and timely delivery of pharmacy care to injured workers. Stakeholders throughout the country contemplated price, the type of medication, where and how they are delivered, and how their use is impacting the duration of a disability and the injured worker's ultimate return to work. Our government affairs team was an active participant in these activities. By sharing insight and perspective on the issues highlighted in this section (as well as others), we were a catalyst for compromise and an advocate for positive change.

Closed Formularies

In September of 2013, the **Texas** closed formulary, based on Official Disability Guidelines (ODG), passed its two-year mark and became fully operational for all claims. The ODG formulary contains a list of drugs ("N" Drugs) that require prior authorization before they can be prescribed. "N" drugs include most opioid analgesics and other medications that have been prone to overuse or abuse. Recently released **Texas** data suggests that the closed formulary is achieving significant results by reducing the prescribing and use of "N" drugs by over 70% and trimming the reimbursement for these drugs by over 80%. **Oklahoma** was the first state to follow the lead of **Texas** and adopted a closed formulary that took effect February 1, 2014. **Oklahoma** allows for the screening of some drugs that are included in the formulary to prevent unrelated medications and compounds from slipping through the system. **Louisiana** and **California** have both publicly announced that they are looking at adopting a closed formulary and other states are evaluating the idea.

Compounded Medications

Following the tragic deaths in 2012 that were attributed to contaminated medications from a compounding pharmacy, the FDA has called for stricter controls and many states are questioning the efficacy and cost of compounded medications that are being prescribed in their workers' compensation systems. For example, **Oklahoma** recently enacted guidelines requiring pre-authorization for all compounded medications as part of their closed formulary. **Mississippi** recently adopted a challenging rule addressing how compounded medications can be billed and when they should be pre-authorized. Specifically, the rule places a $300 limit for 120 grams per compound in a 30-day period. Once the $300 or 120 gram threshold has been met, the compound requires pre-authorization. We anticipate that the scrutiny surrounding compounded medications will continue at both the federal and state levels in 2014.

Medication Rescheduling

The rescheduling of certain drugs is a growing trend in states trying to curtail the use of addictive prescription medications. The most common change is moving hydrocodone products from Schedule III to Schedule II, effectively restricting the ability for injured workers to receive a refill on an existing prescription. **West Virginia** passed legislation this year to move hydrocodone products to Schedule II. **Louisiana** is considering similar legislation. On April 28, 2014, the DEA closed its public comment period on its proposed rule to move all hydrocodone products to Schedule II.

Opioid Analgesics

Suffice it to say, opioids and finding an effective means of curbing their misuse and abuse, was and will continue to be a key focus for stakeholders throughout the system.

- The **Ohio Bureau of Workers' Compensation (BWC)** took a unique approach by adopting standard dose weaning schedules for opiates and a specific set of benzodiazepines. The rule allows for the denial of payments for any medications used outside of the published weaning schedule. These rules took effect April 10, 2014, and impact both BWC-insured employers and self-insured employers.
- **Arizona** passed legislation requiring pre-authorization, a medication agreement and random drug testing any time a Schedule II medication is prescribed.
- **Florida** and **Alaska** introduced legislation that would require drug testing.
- **West Virginia** introduced legislation that would ban the use of non-abuse-deterrent hydrocodone products.
- Meanwhile, several other states, including **Virginia** and **New Jersey**, imposed stricter requirements on health care practitioners to verify a patient's drug use history prior to prescribing or dispensing opioids.
- The FDA continues to refine its Risk Evaluation and Mitigation Strategies process to provide more informative guidance to physicians who prescribe opioids.

The result of these combined efforts is encouraging to policy makers as the use of opioids seems to have reached a plateau, if not already started on the decline, as demonstrated by the 5% reduction in utilization and 6% reduction in the prescription cost per claim of opioid analgesics (see Opioid Analgesics and Morphine Equivalent Dose, page 13). Accordingly, states will continue to seek innovative solutions and legislators and regulators will also continue to refine current tools in an effort to achieve better outcomes.

One such emerging area is drug testing. There has been a marked increase in testing in physician offices and the costs for such testing are escalating. Insurance carriers and self-insured administrators are taking a harder look at the value of such testing and the cost. Some states, like **Delaware**, have enacted legislation controlling the number and the cost of such tests. Drug testing, done properly, can be an effective tool for controlling the misuse and diversion of opioids, but it must be managed carefully to prevent overuse and loss of credibility.

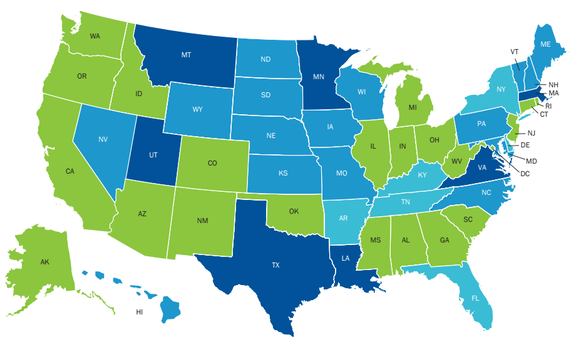
Pharmacy Choice

While most states don't allow for strict direction of care, many do recognize and allow for the voluntary use of networks by injured workers. One of the best tools for controlling pharmacy costs is the use of a managed care network. The choice bills, as proposed, would move states away from encouraging managed care at a time when the health care industry as a whole is embracing it. The use of networks is at an all-time high and this legislation could undermine the positive results that managed pharmacy care has delivered to various states' workers' compensation systems. Eight states — **Alabama, Arizona, Iowa, Maryland, Mississippi, Missouri, New York,** and **West Virginia** — have introduced legislation and several others are thought to be considering the issue.

Physician Dispensing/Repackaged Medications

Physician dispensing of repackaged medications continues to challenge workers' compensation systems around the country. Several states have proposed and some have passed legislation or regulation to help address this challenge.

- In **Florida**, Senator Alan Hays crafted a compromise that garnered enough votes for SB 662 to pass the House and Senate. The bill restricts reimbursement for repackaged medications dispensed by a physician to 112.5% of the AWP of the drug as set by the original manufacturer of the underlying drug used in the repackaging, plus an $8 dispensing fee.
- **Delaware** passed HB 175, which directs the Health Care Advisory Panel to develop rules restricting reimbursement for repackaged medications. The adopted rules governed that reimbursements be based on the AWP of the original product. **Idaho** adopted similar rules.
- **Indiana** implemented regulations last year limiting the reimbursement for repackaged drugs based on the original manufacturer's product NDC. The legislature followed up in 2014 by passing a bill that would limit the time a physician could dispense medications to seven days following the date of injury.
- **Maryland** and **Hawaii** made renewed attempts at moving legislation to limit reimbursement for repackaged drugs but adjourned without passing any restrictions.
- The **Pennsylvania** Assembly recently passed a bill that would limit reimbursement for repackaged medications based on the AWP of the original manufacturer's product and would impose time limits on physician dispensing. That legislation is now awaiting action in the Senate.
- **Louisiana** will attempt to make some changes to their fee schedule, either by rule or by legislation that would rein in repackaged drug costs. Additionally, **Arizona**, **Tennessee,** and **Wisconsin** have bills pending which deal with physician-dispensed medications.
- **Utah** passed legislation that would give limited dispensing authority to doctors. The new authority is limited to oncology medications and injectable cosmetic drugs, but watch for the authority to broaden in coming years.



Restrictions on dispensing, billing and/or reimbursement process
No clear legal or workers' compensation limits on physician dispensing and/or repackaging
Legal restrictions (Practice Act) in addition to workers' compensation controls
Legal restrictions on physician dispensing (denotes Medical/ Pharmacy Act restrictions on all physicians)

Note: States such as AR, FL, NY, and TN have overlapping workers' compensation and state workers' compensation and state "Practice Act" controls.

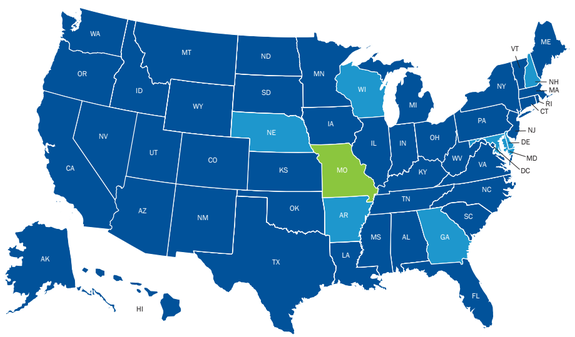
Data reflects published state statues/regulations/case law on physician dispensing/repackaging, current as of January 2014.

Prescription Drug Monitoring Programs (PDMPs)

A number of states have been re-tooling their PDMPs while others have been putting some additional financial resources into their programs to enhance enforcement and educational efforts.

- **New York's** I-STOP program went into effect in August, 2013. In February, 2014, state officials announced that, since its launch, the program has been used by 66,000 health care providers who initiated checks on more than seven million prescriptions. Governor Cuomo noted that the program has already had a significant impact on prescription drug abuse in **New York**.
- **Missouri** attempted to pass legislation to create a PDMP, but due to a filibuster in the Senate, the legislation ultimately failed. **Missouri** therefore remains the lone state without a PDMP.
- **Alaska**, **Florida**, **Maine**, and **Nebraska** moved legislation to add additional funding to expand the reach of their PDMPs. Meanwhile, **Arizona**, **California**, **Colorado**, **Idaho**, **Indiana**, **Louisiana**, **Mississippi**, **New Jersey**, **Pennsylvania**, **Tennessee** and **Wisconsin** were among the states that passed legislation to encourage more participation in their PDMPs by requiring physicians and pharmacists to consult the database prior to prescribing or dispensing or by allowing for more health care professionals to have access to the PDMP.
- A number of states, including **Maryland**, **Minnesota**, **Ohio** and **Virginia**, pushed legislation to allow their PDMPs to be shared across states lines.

At the federal level, Congress is working on legislation titled the National All Schedules Prescription Electronic Reporting Reauthorization Act that would reauthorize the federal controlled substance monitoring program and would help foster the establishment of state-administered controlled substance monitoring programs. Congress is working on the Increasing the Safety of Prescription Drug Use Act that would develop a federal PDMP and help states provide more real-time data related to individuals receiving controlled prescription drugs. We anticipate that the coming year will see continued, sustained activity around PDMPs as states work to make these more viable tools in combating prescription drug abuse.



Operational PDMP
Enacted legislation, PDMP not yet operational
No PDMP

Current as of April 2014

Public Policy

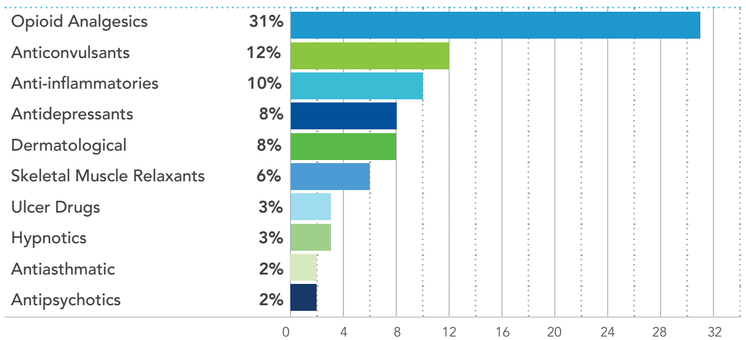
As 2014 is an election year, most state legislators will be running for re-election and will be looking for issues to help position them favorably in the minds of their constituents. Healthcare reform and the implementation of the Affordable Care Act will also draw attention to medical care issues and some of that attention will spill over into workers' compensation. The sluggish economy in many states will also be a factor as governors and policy makers work to develop policies that will attract businesses and jobs to their states. Workers' compensation costs are frequently considered in those policies. Businesses will also be looking at ways to cut the cost of doing business. This will also put pressure on workers' compensation rates, and pharmacy costs will be scrutinized.

“We continue to be encouraged by the ongoing shift in product mix away from long-term opioid analgesics.”

THERAPEUTIC CLASSES

The ranking of the top 10 therapeutic classes as a percentage of total spend is largely unchanged from 2012. Similarly, the top 10 classes continue to represent 90% of the overall spend. And we continue to be encouraged by the ongoing shift in product mix away from long-term opioid analgesics (overall spend was down 7.2%). In addition, we are pleased to see a positive overall trend in generic utilization (76% in 2013). Conversely, increases in the dermatologics therapeutic class is a trend we will continue to monitor closely. A closer look at the top five therapeutic classes, which represent 69% of total spend, along with a review of other noteworthy medication-related topics, follows.

2013 Top Therapeutic Classes as a Percentage of Total Spend



Opioid Analgesics

(Medications in this therapeutic class are commonly used to treat pain in the acute and chronic injury periods. Short-acting opioid analgesics are typically used for moderate to severe pain in the initial stages of injury, while long-acting products are used for baseline treatment of chronic pain.)

Opana® ER, a long-acting product, decreased overall in spend and utilization, perhaps related to the issues with the product reformulation only being crush resistant, and not fully abuse resistant/deterrent, leading prescribers to use OxyContin® which does have abuse deterrent properties in its current formulation.

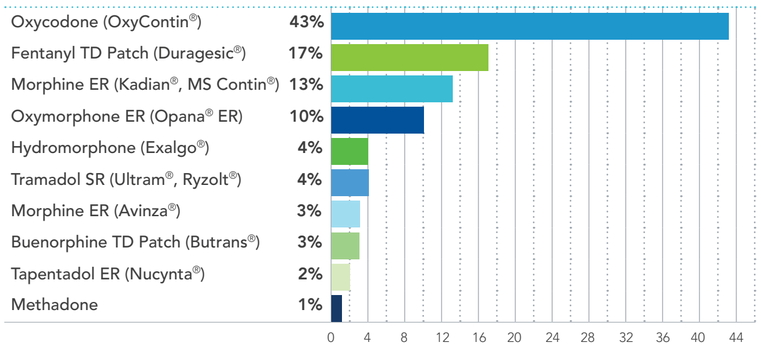
Other more recently approved long-acting formulations (such as Exalgo® and Butrans®) have also found a place in the workers' compensation population, increasing in utilization. The overall effect was a change in medication distribution from existing long-acting products to other medications, not an increase in expenditures for the therapeutic class.

Since 2009, there have been four long-acting opioid analgesics added to the market. These agents include:

- Embeda® (morphine-naltrexone) released in fourth quarter 2009, but subsequently taken off the market in 2011 due to safety concerns regarding the sustained-release formulation
- Exalgo® (extended-release hydromorphone) released in third quarter 2010
- Butrans® (buprenorphine patch) released in second quarter 2011
- Nucynta® ER (extended-release tapentadol) released fourth quarter 2011

Based on our pharmacy spend, the entry of these new formulations into the market did not lead to a significant change in total utilization of long-acting opioid analgesics based on total transactions and days' supply compared to total opioid analgesic use.

2013 Top Long-acting Opioid Analgesics Ranked by Total Opioid Spend



What this means to you

The availability of new long-acting opioid analgesic formulations over the last few years did not result in an overall increase in spend or utilization. And fortunately (as discussed earlier in this report) overall use of opioid analgesics is down. This leads us to a point of emphasis — the ongoing focus must remain on ensuring the opioid therapy regimen is effective.

The clinical tools and resources we provide our clients empower claims professionals to make more informed decisions at every stage of the claim while the application of global utilization management strategies emphasize prevention, patient safety, and collaboration to help ensure the injured worker receives the right medication at the right time. Working alongside our clients, we can continue to achieve better outcomes.

Anticonvulsants

(Medications in this therapeutic class are typically used in workers' compensation for the treatment of neuropathic (nerve) pain, a condition frequently seen with chronic pain.)

The utilization of gabapentin is increasing for the treatment of pain in the injured worker. One of the possible explanations is the availability of newer long-acting formulations that are better tolerated by patients. Gralise™ and Horizant™ are technically considered in the therapeutic class of miscellaneous psychotherapeutics, but the formulation is being used off-label for the treatment of neuropathic pain. The doses of gabapentin (immediate-release) and Gralise (sustained-release) were nearly equivalent on the average mg/day prescribed to claimants (1409 mg vs 1463 mg per day). This is surprising, given that, in theory, the Gralise formulation would be able to provide the same benefit at a lower dose.

Pregabalin, known by the brand name Lyrica®, moved from number three to number four in the top 100 by total spend, most likely substituting for the aforementioned gabapentin products, or possibly switching to therapy with Cymbalta® (duloxetine).

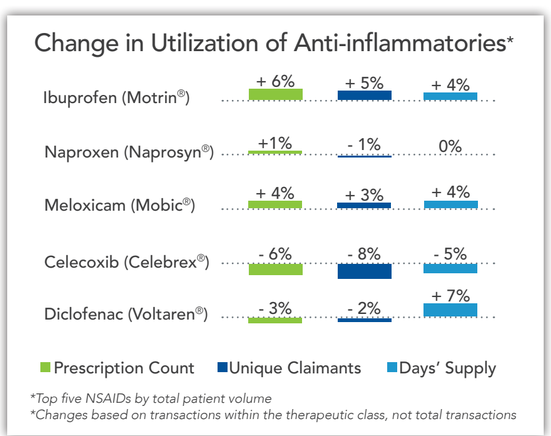
What this means to you

The increased use of gabapentin formulations demonstrates that prescribers are treating injured workers diagnosed with chronic pain by using adjunctive medications in an effort to reduce the use of long-term opioid analgesics.

Anti-inflammatories

(Anti-inflammatories are most commonly used in workers' compensation for the treatment of pain and inflammation caused by injuries.)

Celebrex® continues to lose ground against other generically available non-steriodal anti-inflammatory medications (NSAIDs). Last year we reported a 14% decrease in the number of claimants receiving Celebrex; 2013 showed an 8% decrease in year-over-year claimant volume. The shift was in favor of other NSAIDs available in generic formulation. These generic NSAIDs are also considered first-line therapy for the treatment of pain and inflammation, and should be used before moving to a more expensive therapy. Interestingly enough, there was not a corresponding increase in the use of proton pump inhibitors (PPIs) like omeprazole (Prilosec®), which are commonly used in combination therapy with NSAIDs to decrease the risk of gastrointestinal bleeding for prolonged treatment.



What this means to you

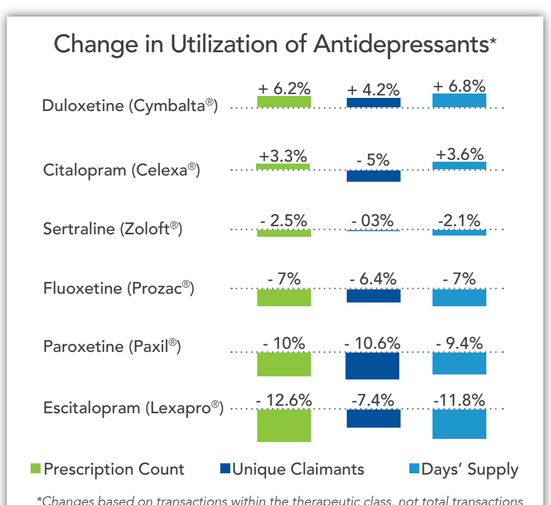
The shift away from brand name Celebrex towards other generic NSAIDs has a favorable impact on spend and can more positively influence patient safety in some circumstances.

Antidepressants

(This class of drugs is primarily used in workers' compensation for the treatment of nerve pain associated with chronic injuries as well as the treatment of depression that can coexist with chronic pain.)

Antidepressant medications are used in the management of depression, which is often secondary to occupational injuries. Depression is also a common condition in patients with chronic pain and typically requires multi-modal treatments with medications and cognitive therapies.

Since Cymbalta® received an FDA approval for chronic musculoskeletal pain in November 2010, it has become the primary antidepressant used for the treatment of pain and/or depression in the injured worker population. Overall, the use of antidepressants has only increased slightly in the industry, with Cymbalta leading market share. The antidepressant class that has had the greatest impact is the selective serotonin reuptake inhibitors (SSRIs). The SSRIs are only approved for anxiety and depression with limited evidence in the off-label treatment of pain.



What this means to you

The increased use of Cymbalta, and its generic duloxetine, demonstrates that prescribers are treating injured workers with chronic pain by using fewer opioid medications, and turning to alternatives for medication therapy. Furthermore, since duloxetine has the dual indication for treating both pain and depression, it has become the primary antidepressant for such diagnosed claimants when depression is identified as a comorbid condition related or otherwise attributed to the injury.

Dermatologics

(This product class includes medications that are applied externally to the skin for the treatment of infection, inflammation, and pain relief.)

In the recent past, the dermatologic class has predominantly consisted of lidocaine 5% patches (Lidoderm®). Although the majority of spend and utilization is still associated with Lidoderm, or its generic, it stays high on the leader board, taking the number two spot for overall individual medication spend.

There has also been a dramatic increase in the appearance of other topical formulations, such as Medrox®, New Terocin®, Dendracin®, and Medi-Derm®. These formulations contain multiple anti-inflammatory, analgesic, and inert ingredients. It appears that the increased utilization of dermatologics as part of the medication therapy regimen is related to the prevailing thought that topical formulations are applied and absorbed only where needed, and thus produce less systemic exposure to a drug. However, the clinical evidence of topical formulations as safer and more effective than oral medications is lacking.

The commercially available formulations with the largest increases in spend and utilization are the products containing the three ingredients capsaicin, menthol, and methyl salicylate in various concentrations. These products have doubled in use over the last year, and currently rank 76th by total spend (up from 105th in total spend in 2012).

It is likely that the increased use of these commercially available topical formulations mirror the increased spend and utilization the workers' compensation industry has seen with compounded medications.

What this means to you

Topical formulations, whether available commercially or as a compounded medication, should be monitored closely to ensure safe and effective use.

Skeletal Muscle Relaxants

(This type of muscle relaxant is typically used for the treatment of muscle spasms that frequently accompany occupational injuries, such as sprains or strains.)

The most notable trend associated with this therapeutic class is the ongoing decrease in use of carisoprodol (Soma®). In 2013 the utilization of carisoprodol dropped by 15.2%. Similar to benzodiazepines, carisoprodol is not recommended for long-term use due to short-term benefits, drug-to-drug interactions and the high potential risk of abuse and dependence. Also worthy of note is movement in rank of two other skeletal muscle relaxants, metaxalone and cyclobenzaprine. Each medication dropped two spots, moving from 11th to 13th and 17th to 19th, respectively. This movement highlights changing prescribing habits influenced by evidence-based medicine and utilization management.

What this means to you

The decreasing use of skeletal muscle relaxants and their wide generic availability are two factors contributing to lower costs in this therapeutic class. We will continue to support the appropriate use of these medications to help ensure this positive trend continues.

Hypnotics

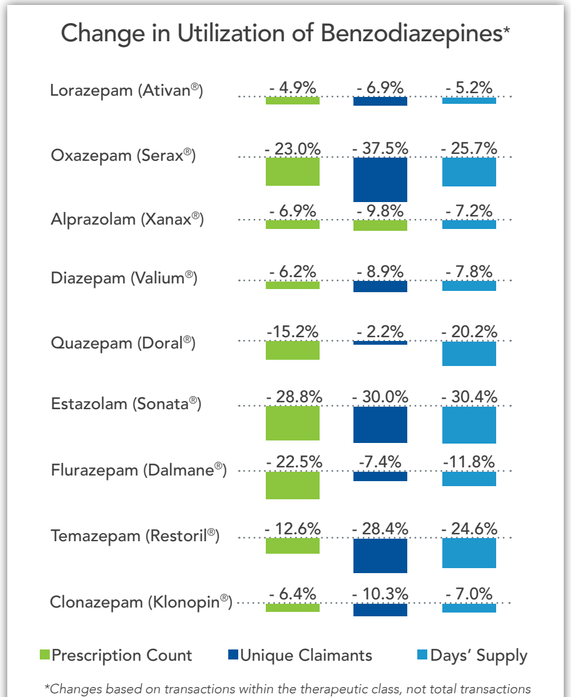
(Typically used in workers' compensation for the treatment of insomnia and sleep disorders.)

The use of hypnotics has dropped from 3.3% to 2.9% of total transactions. The decrease may be partially attributed to changes in utilization of benzodiazepines. Interestingly, the utilization of non-benzodiazepine sedatives escopiclone (Lunesta®) and zolpidem (Ambien®, Ambien® CR) did not change; thus it would appear that prescribers are writing fewer prescriptions for hypnotics and not just replacing benzodiazepines.

Benzodiazepines

(Included medications found in several therapeutic classes, and are commonly used for the treatment of acute anxiety, insomnia, seizure disorders, and muscle spasms.)

Benzodiazepines have had an overall reduction in use and duration of therapy in 2013. Although benzodiazepines can be effective for the short-term treatment of several conditions, they are not recommended for long-term use because efficacy is unproven. It has been shown that extended use can increase risk of psychological and physical dependence and addiction. Additionally, benzodiazepines potentiate the effects of other drugs, such as opioids analgesics, which can result in severe adverse medical events. Nearly all clinical guidelines recommend against long term use of benzodiazepines. Specifically, ODG considers all benzodiazepines as non-formulary in their drug chapter.



What this means to you

The decrease in total transactions for hypnotics is positive; as is the shift away from benzodiazepines. As these medications are seen frequently in our book of business in specific claims, ongoing monitoring and management of chronic use is recommended. It is important that claimants be managed carefully to avoid dependence, tolerance, and addiction. Furthermore, it is also suggested that non-pharmacologic therapies be considered in tandem with the overall medication therapy.

“Making workers’ compensation better, together.”

LOOKING AHEAD

The value a pharmacy benefit manager delivers to its client is evaluated in a variety of ways. Unit cost (transactional) savings is amongst the more common measurements. And while the price per prescription is a valid point of comparison of one pharmacy benefit manager to another, it overlooks the fact that even the lowest price per prescription is too much to pay when the prescription never should have been filled in the first place.

As outlined by this report, we have a knack for cost containment and a passion for our business. Ensuring the right decision is made so that the injured worker receives the right medication at the right time, while the payer protects their financial interest is not easy. It requires a balanced and unbiased perspective, veteran clinical expertise, keen analytic insight, and a strong moral compass — because sometimes the right decision — is a difficult one. As we look ahead to 2014 and beyond, we do not foresee any of today's challenges going away; rather we will become even more adept at mitigating their influence. Through ongoing collaboration, product innovation, and service enhancements we, in conjunction with our clients, will continue to make our industry better, together.

APPENDIX

New Medications, Indications and Generic Formulations

Significant medication approvals, launches, and memorable FDA rulings helped shape the direction of pain management and subsequently, workers' compensation in 2013. The time line below walks you through the more notable market happenings and paves the way for 2014.

2013

JANUARY

Opana® ER tablet (oxymorphone extended-release)

Impax announced in early January 2013 that it had commenced shipping its generic version of Opana ER. It is important to note that Impax's generic oxymorphone extended-release tablet does not possess abuse-deterrent characteristics. Therefore, this product has the potential for inappropriate use and is not considered a true generic equivalent, but rather, a generic alternative. In May 2013, the FDA affirmed its decision to allow generic non-abuse deterrent extended-release oxymorphone on the market despite a Citizen's Petition issued by Endo Pharmaceuticals, Inc., the original manufacturer of brand-name, Opana ER.

Lamictal® XR (lamotrigine)

The extended-release version of Lamictal was released as a generic drug product in early 2013. Due to its side-effect profile and slow titration period, lamotrigine is not considered a first-line therapy option for neuropathic pain; however, it may be an option in patients who fail to respond to first-line agents.

Botox® solution for injection (onabotulinumtoxinA)

The FDA expanded the approved indications list for Botox to include the treatment of overactive bladder, a condition previously treated mainly with oral therapy. Although not commonly seen in workers' compensation, it is possible that patients suffering from spinal cord injuries may require treatment for bladder dysfunction, thus rendering Botox a possible therapeutic option. Aside from overactive bladder, Botox is most commonly seen in the pain management/workers' compensation population for the prevention of migraine headaches.

Zecuity® transdermal iontophoretic patch (sumatriptan)

In early 2013 NuPathe Inc. announced that it had received FDA approval for its novel anti-migraine patch, Zecuity, indicated for the treatment of acute migraine headaches. Zecuity, a battery-powered patch, delivers medication to the bloodstream via the skin with the use of a mild electrical current. Although the manufacturer anticipated releasing the product in 2013, a launch date of early 2014 is now planned as NuPathe Inc. attempts to secure a marketing partner for this product.

MARCH

Reclast® (zoledronic acid)

Reclast was released last year as a generic drug product approved for the treatment of various conditions, including osteoporosis treatment and prevention. Reclast is an injectable drug product and is intended to be administered once yearly.

Concerta® (methylphenidate) 36 mg and 54 mg

After releasing a generic version of the 27 mg dosage strength in December 2012, Mallinckrodt released additional dosage strengths (36 mg and 54 mg) in generic versions in early 2013. Although FDA-indicated for the treatment of attention-deficit hyperactivity disorder (ADHD) and narcolepsy, stimulant medications are often used for the treatment of opioid-induced sedation and refractory depression in an off-label fashion, as well as for the treatment of cognitive impairment following traumatic brain injuries (TBI).

APRIL

Amitiza® (lubiprostone)

Sucampo Pharmaceuticals, Inc. announced earlier last year that the FDA had approved Amitiza for the treatment of opioid-induced constipation in patients with chronic, non-cancer pain. The approval of Amitiza for this indication marked the first oral medication specifically approved for the treatment of constipation related to opioid therapy. Amitiza is currently available as a brand-only product.

FDA blocks generic OxyContin® (extended-release oxycodone) from entering market

Following concerns over patient safety and a potential increase in opioid abuse, the FDA ruled in early 2013 that generic versions of non crush-resistant OxyContin would not be allowed on the market. Currently, the patent for crush-resistant OxyContin is not set to expire until at least 2025.

AUGUST

Focalin® XR (dexmethylphenidate)

Used off-label in the pain management population for the treatment of medication-induced sedation, the FDA approved a generic version of this long-acting stimulant in mid/late 2013. Given the transient nature of most medication-related adverse effects (e.g. sedation, cognitive impairment), the use of chronic stimulants is usually not recommended for patients.

SEPTEMBER

Brintellix® (vortioxetine)

Takeda and Lundbeck recently announced the FDA's approval of the antidepressant, Brintellix. This medication is FDA-indicated for the treatment of major depressive disorder (MDD). A launch is expected in the second half of 2014.

Lidoderm® (topical lidocaine patches)

FDA-indicated for the treatment of nerve pain following shingles (post-herpetic neuralgia), and used extensively in pain management for the off-label treatment of generalized neuropathic pain, Lidoderm is now available as a generic equivalent from Actavis, Inc. Clinical guidelines still recommend the use of first-line agents (e.g. gabapentin, amitriptyline, etc.) for the treatment of generalized neuropathic pain before considering a trial of topical lidocaine patch therapy.

Khedezla® (desvenlafaxine)

Par Pharmaceuticals of Woodcliff Lake, NJ announced the launch of Khedezla, an antidepressant medication in the SNRI class. Although Khedezla contains the same active ingredient as competitor product Pristiq®, the two are not considered product substitutions for each other. Khedezla is currently FDA-indicated for the treatment of major depressive disorder (MDD)

Zubsolv® (buprenorphine/naloxone)

Orexo's Zubsolv is now commercially available in the United States in 1.4 mg/0.36 mg and 5.7 mg/1.4 mg strengths as of late 2013. Zubsolv is FDA approved for the treatment of opioid dependence; however, it is possible that prescribers may use this agent for chronic pain management in an off-label manner.

Trokendi XR™ (topiramate extended-release)

Supernus Pharmaceuticals announced its launch of the first, once-daily formulation of topiramate, an anticonvulsant medication used in the treatment of seizure disorders. Used as a second-line treatment option in the off-label management of neuropathic pain, this once daily formulation appears to offer no significant clinical advantage to currently available generic topiramate products.

Butrans® (buprenorphine 15 mcg/hr patch)

Already available in 5 mcg/hr, 10 mcg/hr, and 20 mcg/hr strengths since its 2010 approval, Purdue Pharma's recently launched a 15 mcg/hr strength patch. Butrans is currently FDA indicated for the treatment of pain severe enough to require around-the-clock treatment and for which alternative therapies have been inadequate.

2013

OCTOBER

Zohydro® ER (hydrocodone extended-release)

Following its approval by the FDA on October 25, 2013, Zohydro ER became the first extended-release hydrocodone-only pain reliever available in the United States. Previously, hydrocodone was only available in combination products with non-opioid constituents (such as acetaminophen and ibuprofen).

Although the FDA appeared to be on a path of requiring all new opioid products to have abuse resistant or deterrent features, Zohydro ER does not possess any abuse-deterrent properties. This notwithstanding, the FDA does indicate that post-marketing surveillance studies regarding the medication's susceptibility to abuse, addiction, and misuse will be required and a REMS will be required in accordance with their 2012 mandate. Zogenix, the manufacturer of Zohydro ER, also indicates that an External Safe-Use Board consisting of pain specialists and addictionologists has been developed to aid in this task and to ensure that all safety data are considered and presented to the manufacturer's Board of Directors. The manufacturer further indicates that an abuse-deterrent formulation is currently being developed and will likely become available within the next three years pending FDA approval.

NOVEMBER

AcipHex® (rabeprazole)

The FDA recently approved generic versions of AcipHex from various generic drug manufacturers for the treatment of gastroesophageal reflux disease (GERD). Although this particular product is not currently utilized extensively in the workers' compensation population, its generic status may make it a more attractive, cost effective alternative to other brand-only products.

Embeda® (morphine-naltrexone)

After it voluntarily recalled Embeda from the market in early 2011, Pfizer recently indicated that Embeda would once again be released onto the United States market for the treatment of pain requiring around-the-clock coverage. Pfizer anticipates that Embeda will become commercially available in second quarter 2014.

DECEMBER

Esomezol (esomeprazole strontium, delayed release)

Manufactured by Korea's Hanmi Pharmaceutical Company, Esomezol is a proton-pump inhibitor FDA indicated for the treatment of gastroesophageal reflux disease, NSAID-induced gastric ulcer, and other gastrointestinal conditions. Although Esomezol contains the same active ingredient as Nexium®, a small difference in the formulation of the product means the two are not interchangeable (i.e., one may not be substituted for the other without a new prescription). Currently, there are no studies indicating any clinical advantage for Esomezol over existing proton-pump inhibitor alternatives on the market.

Fetzima® (levomilnacipran)

Forest Laboratories, Inc. announced the successful FDA approval of levomilnacipran, a selective norepinephrine-serotonin reuptake inhibitor indicated for the treatment of major depressive disorder. Fetzima's mechanism of action is similar to that of Savella® (milnacipran); although Savella® is only FDA approved for the treatment of fibromyalgia in the United States.

Cymbalta® (duloxetine)

The FDA approved a generic version of Cymbalta (duloxetine) from several generic drug manufacturers. Much like the brand name product, generic duloxetine is available in 20 mg, 30 mg, and 60 mg capsules. Duloxetine is used extensively in the treatment of pain and depression/anxiety in workers' compensation.

Figure 1

Top 25 Medications as a Percentage of Total Spend with AWP

2013 Rank	2012 Rank	Total	Common Brand Name	Changes in AWP Brand and Generic	Changes in AWP Brand Only
1	1	7.60%	OxyContin® tablet	+ 4.5%	+ 4.5%
2	2	5.30%	Lidoderm® patch	+ 14.7%	+ 14.8%
3	4	5.12%	Cymbalta® capsule	+ 19.7%	+ 19.7%
4	3	5.09%	Lyrica® capsule	+ 19.5%	+ 19.5%
5	6	3.98%	Celebrex® capsule	+ 19.2%	+ 19.2%
6	5	3.81%	Norco® tablet	+ 4.9%	+ 13.6%
7	7	3.38%	Percocet® tablet*	+ 5.4%	+ 23.6%
8	8	2.69%	Duragesic® patch*	+ 2.0%	+ 8.6%
9	9	2.03%	Neurontin® tablet*	+ 0.1%	+ 12.7%
10	10	1.85%	Neurontin® capsule*	+ 2.8%	+ 57.4%
11	14	1.65%	Opana® ER tablet*	+ 2.4%	+ 3.9%
12	12	1.50%	Mobic® tablet*	+ 1.1%	– 1.5%
13	11	1.40%	Metaxalone® tablet	+ 4.7%	+ 3.9%
14	13	1.37%	Ultram® tablet*	+ 0.9%	+ 10.1%
15	15	1.27%	Roxicodone® tablet*	+ 0.5%	+ 10.5%
16	16	1.26%	Flector® patch	+ 13.2%	+ 13.2%
17	19	1.07%	Fexmid tablet	– 5.2%	– 7.0%
18	26	1.01%	Abilify® tablet	+ 16.3%	+ 16.3%
19	20	1.00%	Ambien® tablet*	+ 1.4%	+ 20.8%
20	21	0.99%	Topamax® tablet*	+ 0.8%	+ 9.5%
21	56	0.97%	Ketamine® HCL powder	+ 33.1%	+ 33.3%
22	24	0.97%	Nexium® capsule	+ 11.4%	+ 11.4%
23	18	0.94%	Kadian® capsule*	+ 0.0%	+ 9.1%
24	23	0.94%	MS Contin® tablet*	– 0.1%	+ 6.0%
25	17	0.93%	Provigil® tablet*	+ 7.9%	+ 33.8%

**Signals generic availability*

Figure 2

Top 25 Medications by Percentage of Total Rx with AWP

2013 Rank	2012 Rank	Total	Common Brand Name	Changes in AWP Brand and Generic	Changes in AWP Brand Only
1	1	14.37%	Norco® tablet	+ 4.9%	+ 13.6%
2	2	4.52%	Percocet® tablet*	+ 5.4%	+ 23.6%
3	3	3.99%	Ultram® tablet*	+ 0.9%	+ 10.1%
4	4	3.72%	Fexmid tablet	– 5.2%	– 7.0%
5	5	3.32%	ibuprofen tablet	+ 2.9%	– 26.8%
6	7	2.64%	Neurontin® capsule*	+ 2.8%	+ 57.4%
7	6	2.58%	Lyrica® capsule	+ 19.5%	+ 19.5%
8	9	2.35%	Cymbalta® capsule	+ 19.7%	+ 19.7%
9	10	2.31%	Roxicodone® tablet*	+ 0.5%	+ 10.5%
10	8	2.29%	Celebrex® tablet	+ 19.2%	+ 19.2%
11	11	1.96%	OxyContin® tablet	+ 4.5%	+ 4.5%
12	14	1.94%	Mobic® tablet*	+ 1.1%	– 1.5%
13	13	1.78%	Lidoderm® patch	+ 14.7%	+ 14.8%
14	12	1.72%	carisoprodol tablet	– 3.9%	+ 3.9%
15	15	1.69%	Naprosyn® tablet	+ 0.1%	+ 7.8%
16	17	1.57%	Zanaflex® tablet*	+ 2.1%	+ 1.6%
17	16	1.41%	Ambien® tablet*	+ 1.4%	+ 20.8%
18	18	1.36%	Neurontin® tablet*	+ 0.1%	+ 12.7%
19	19	1.15%	diazepam tablet	– 3.3%	+ 8.6%
20	20	1.00%	alprazolam tablet	+ 3.1%	+ 16.3%
21	22	0.99%	amitriptyline tablet	– 2.2%	+ 23.6%
22	21	0.97%	Duragesic® patch*	+ 2.0%	+ 8.6%
23	23	0.95%	Robaxin® tablet	+ 6.8%	– 5.9%
24	25	0.90%	omeprazole capsule	+ 0.1%	+ 9.7%
25	24	0.89%	MS Contin® tablet*	– 0.1%	+ 6.0%

**Signals generic availability*

Figure 3

Top 25 Medications Ranked by Daily Spend

2013 Rank	2012 Rank	Medication	2013 Daily Spend	2012 Daily Spend	Change
1	1	Fentora® tablet	$ 345.90	$ 281.30	+ 23.0%
2	2	Ketamine® powder	$ 74.10	$ 49.39	+ 50.0%
3	3	Gabapentin® powder	$ 62.45	$ 47.97	+ 30.2%
4	4	Duragesic® patch*	$ 38.51	$ 35.72	+ 7.8%
5	5	Exalgo® ER tablet	$ 32.69	$ 28.13	+ 16.2%
6	6	Magnacet® tablet	$ 33.79	$ 27.46	+ 23.0%
7	7	Kadian® capsule*	$ 29.14	$ 25.92	+ 12.4%
8	8	Abilify® tablet	$ 27.76	$ 24.27	+ 14.4%
9	9	Opana® ER tablet*	$ 24.04	$ 24.16	– 0.5%
10	10	OxyContin® tablet	$ 22.56	$ 22.08	+ 2.2%
11	11	Amrix® capsule	$ 27.07	$ 17.59	+ 53.9%
12	12	Avinza® capsule	$ 18.93	$ 16.41	+ 15.4%
13	13	Lidoderm® patch	$ 16.01	$ 14.14	+ 13.2%
14	14	Skelaxin® tablet*	$ 13.46	$ 13.03	+ 3.3%
15	15	Flector® patch	$ 14.66	$ 12.98	+ 13.0%
16	16	Nucynta® tablet	$ 12.17	$ 11.72	+ 3.9%
17	17	Butrans® patch	$ 11.15	$ 9.94	+ 12.2%
18	18	Advair® diskus	$ 11.12	$ 9.85	+ 12.9%
19	19	Cymbalta® capsule	$ 10.86	$ 9.15	+ 18.7%
20	20	Lorcet® tablet*	$ 10.29	$ 8.88	+ 15.8%
21	21	Lyrica® capsule	$ 10.19	$ 8.53	+ 19.5%
22	22	Nexium® capsule	$ 9.51	$ 8.52	+ 11.6%
23	23	Lunesta® tablet	$ 9.45	$ 8.25	+ 14.5%
24	24	Celebrex® capsule	$ 8.36	$ 7.05	+ 18.5%
25	25	Voltaren® gel	$ 4.32	$ 3.99	+ 8.3%

**Signals generic availability*

Figure 4

AWP Inflation — Top 25 Brand Medications*

2013 Rank	Medication	Inflation Rate
1	OxyContin® tablet	+ 5%
2	Lidoderm® patch	+ 15%
3	Cymbalta® capsule	+ 20%
4	Lyrica® capsule	+ 20%
5	Celebrex® capsule	+ 19%
6	Opana® ER tablet	+ 4%
7	Flector® patch	+ 13%
8	Percocet® tablet	+ 24%
9	Abilify® tablet	+ 15%
10	Nexium® capsule	+ 11%
11	Duragesic® patch	+ 9%
12	Lunesta® tablet	+ 15%
13	Nucynta® tablet	+ 8%
14	Exalgo® tablet	+ 23%
15	Skelaxin® tablet	+ 4%
16	Fentora® tablet	+ 21%
17	Amrix® capsule	+ 54%
18	Avinza® capsule	+ 16%
19	Butrans® patch	+ 13%
20	Advair Diskus®	+ 13%
21	Voltaren® gel	+ 13%
22	Norco® tablet	+ 14%
23	Kadian® capsule	+ 9%
24	Nucynta® ER tablet	+ 9%
25	Spiriva® capsule	+ 8%

**Ranked as a percentage of spend*

Figure 5

AWP Inflation — Top 25 Generic Medications*

2013 Rank	Medication	Inflation Rate
1	hydrocodone/APAP tablet	+ 6%
2	oxycodone/APAP tablet	+ 1%
3	gabapentin tablet	+ 0%
4	fentanyl patch	– 1%
5	gabapentin capsule	+ 0%
6	meloxicam tablet	+ 1%
7	tramadol HCL tablet	+ 1%
8	oxycodone tablet	+ 0%
9	cyclobenzaprine tablet	– 5%
10	tizanidine tablet	+ 2%
11	omeprazole capsule	+ 0%
12	zolpidem tablet	+ 0%
13	topiramate tablet	+ 0%
14	morphine sulfate tablet	+ 3%
15	modafinil tablet	+ 4%
16	metaxalone tablet	+ 7%
17	morphine sulfate capsule	+ 1%
18	naproxen tablet	+ 0%
19	zolpidem ER tablet	+ 0%
20	ondansetron tablet	– 1%
21	tramadol HCL tablet	+ 0%
22	quetiapine tablet	– 4%
23	escitalopram tablet	+ 6%
24	fentanyl OT lozenge	+ 3%
25	venlafaxine capsule	+ 0%

**Ranked as a percentage of spend*

Figure 6

Top 10 Ingredients Found in Compounded Medications*

2013 Rank	2012 Rank	Medication	2013 Daily Spend	2012 Daily Spend	Change	2013 Rank**
1	1	Flurbiprofen® powder	$ 76.84	$ 68.44	+ 12.3%	31
2	2	Ketamine® HCL powder	$ 74.10	$ 49.39	+ 50.0%	11
3	3	Gabapentin® powder	$ 62.45	$ 47.97	+ 30.2%	18
4	11	Bupivacaine® powder HCL	$ 52.25	$ 9.54	+ 447.4%	298
5	8	Baclofen® powder	$ 51.68	$ 29.61	+ 74.5%	66
6	6	Tramadol HCL® powder	$ 46.24	$ 32.77	+ 41.1%	152
7	4	Ketoprofen® powder	$ 45.52	$ 39.30	+ 15.8%	27
8	7	Cyclobenzaprine® powder HCL	$ 43.35	$ 30.52	+ 42.1%	67
9	12	Lidocaine® powder	$ 43.01	$ 9.48	+ 353.6%	547
10	9	Diclofenac® powder	$ 40.55	$ 24.09	+ 68.3%	76

**Ranked based on priced per days' supply*
***2013 rank as a percentage of total spend*

Figure 7

Specialty Medications*

Specialty Medication	Brand Name	Indicated Use	Average Price per Rx
Emtricitabine-Tenofovir	Truvada®	Human Immunodeficiency Virus (HIV)	$ 852.80
Lamivudine-Zidovudine	Combivir®	Human Immunodeficiency Virus (HIV)	$ 496.26
Peginterferon alfa-2a	Pegasys®	Hepatitis B/C	$ 3,002.27
Peginterferon alfa-2b	Peg-Intron®	Hepatitis C	$ 2,909.39
Enoxaparin	Lovenox®	Clotting Disorders	$ 712.79
Golimumab	Symponi®	Rheumatoid Arthritis, Ulcerative Colitis	$ 2,890.13

**Ranked by indicated use*

Figure 8

Top 25 Generic Medications Including Generic Efficiency*

2013 Rank	2012 Rank	Generic Spend	Generic Product Name	Common Brand Name	Generic RX	Utilization
1	1	8.7%	hydrocodone/APAP tablet	Vicodin® tablet, Lortab® tablet	18.5%	98.1%
2	2	5.7%	oxycodone/APAP tablet	Percocet® tablet, Endocet® tablet	5.6%	95.1%
3	4	4.8%	gabapentin tablet	Neurontin® tablet	1.7%	96.9%
4	3	4.5%	fentanyl patch	Duragesic® patch	1.1%	85.7%
5	5	4.3%	gabapentin capsule	Neurontin® capsule	3.4%	97.8%
6	6	3.7%	meloxicam tablet	Mobic® tablet	2.5%	98.4%
7	7	3.3%	tramadol HCL tablet	Ultram® tablet, Ryzold® tablet	5.2%	98.7%
8	8	3.0%	oxycodone tablet	Roxicodone® tablet	3.0%	98.2%
9	9	2.7%	cyclobenzaprine tablet	Flexeril® tablet, Amrix® tablet	5.0%	99.8%
10	11	2.3%	tizanidine tablet	Zanaflex® tablet	2.0%	99.1%
11	14	2.2%	omeprazole capsule	Prilosec® capsule	1.1%	97.9%
12	10	2.1%	zolpidem tablet	Ambien® tablet	1.7%	93.9%
13	12	2.1%	topiramate tablet	Topamax® tablet	0.6%	92.6%
14	13	2.1%	morphine sulfate tablet	MS Contin® tablet	1.1%	96.6%
15	28	1.2%	modafinil tablet	Provigil® tablet	0.1%	86.0%
16	17	1.7%	metaxalone tablet	Skelaxin® tablet	0.5%	49.7%
17	20	1.3%	morphine sulfate capsule	Kadian® capsule	0.2%	66.8%
18	19	1.2%	naproxen tablet	Naprosyn® tablet	2.2%	99.7%
19	16	1.2%	zolpidem ER tablet	Ambien® CR tablet	0.6%	84.4%
20	23	1.2%	ondansetron tablet	Zofran® tablet	0.2%	97.3%
21	18	1.2%	tramadol ER tablet	Ultram® ER tablet	0.5%	93.6%
22	37	1.1%	quetiapine tablet	Seroquel® tablet	0.3%	92.2%
23	32	1.1%	escitalopram tablet	Lexapro® tablet	0.6%	89.6%
24	15	1.0%	fentanyl citrate	Actiq® capsule, Fentora® capsule	0.3%	82.1%
25	22	1.0%	venlafaxine ER capsule	Effexor® XR capsule	0.4%	88.9%

**Ranked based on total spend, generic medications*

Figure 9

Medications with Weight Gain Potential

Medication	Common Brand Names	Therapeutic Class	Population Receiving Medication
Aripiprazole	Abilify®	Antipsychotic	**0.3%**
Pregabalin	Lyrica®	Anticonvulsant	**4.7%**
Olanzapine	Zyprexa®	Antipsychotic	**0.1%**
Quetiapine	Seroquel®, Seroquel® XR	Antipsychotic	**0.4%**
Fluticasone-salmeterol	Advair®	Respiratory agent	**0.4%**
Alprazolam	Xanax®	Antianxiety agent	**1.9%**
Celecoxib	Celebrex®	Anti-inflammatory	**5.7%**
Clonazepam	Klonopin®	Anticonvulsant	**1.2%**
Gabapentin	Neurontin®, Gralise™, Horizant™	Anticonvulsant	**8.9%**
Lamotrigine	Lamictal®	Anticonvulsant	**0.2%**
Desvenlafaxine	Pristiq®	Antidepressant	0.2%
Sertraline	Zoloft®	Antidepressant	0.8%

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