







WINTER 2016

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PUTTING CARE IN THE RIGHT CONTEXT

THE CALIFORNIA DWC FORMULARY ADDS AN IMPORTANT LAYER OF CLINICAL CONTEXT TO GUIDE DRUG THERAPY PRESCRIBING



As chief medical officer at Healthesystems and an occupational medicine expert, a key component of my role is providing clinical direction to guide the development of medical treatment guidelines and workers' compensation policy initiatives that will better serve the needs of injured workers. So it's an exciting moment for me when, as an industry, we can add another tool to our arsenal that puts the patient at the center of treatment decisions.

The draft formulary released in September by the California Department of Workers' Compensation (DWC) is a significant addition to that arsenal. At the highest level, the 2017 implementation means that two of the largest states in the country will have workers' compensation drug formularies (Texas having adopted a closed drug formulary in 2010 that has demonstrated success). Not only will this impact the care of hundreds of thousands of injured workers, it will further increase our capacity to gather data on formulary outcomes that will help us fine-tune best practices for their future development and implementation.

But the proposal is exceptionally significant in that it places an increased emphasis on the quality of care for workers' compensation patients. While the formulary list itself is not directly

diagnosis-driven, it notably is linked to the California Medical Treatment Utilization Schedule (MTUS) and driven by the American College of Occupational and Environmental Medicine (ACOEM) treatment guidelines. The DWC adoption of a closed-drug formulary grounded in such high quality, evidence-based guidelines is extremely important for a number of reasons.

First and foremost, it will enhance the quality and delivery of care, which will provide real benefits to injured workers. The guidelines provide parameters that will help prescribers make drug therapy decisions within the context of the condition or injury being treated, rather than decisions that are based on the availability of medications alone. As prescribers align with guidelines and move to adopt the preferred drugs for the proper conditions, we should expect to see a correlating improvement in clinical outcomes for these patients. In this respect, the formulary represents another large-scale step towards ensuring that drug therapy decisions are made within the right clinical context.

Given this, it seems especially appropriate that many of the articles within this issue of *RxInformer* journal discuss the advantages of having a more complete picture of patient information by which to

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make treatment and claims management decisions. This includes their workplace injury or condition, comorbid conditions that may fall outside of the workers' comp system but directly impact treatment for their work-related injury, and additional data that goes beyond injury to look more broadly at patient characteristics. Notably, the article "Thinking Outside the Claim: Using Multidimensional Data to Estimate Potential Opioid Misuse" on page 20 discusses how a predictive model that considers multidimensional data such as socioeconomic status, gender, age, and employment can better serve to help estimate potential opioid risk across a patient population.

Of course, no matter how many tools we have at our disposal, they are only successful when supported by the everyday excellence of those who are responsible for managing the care of injured workers. That's why we include content in RxInformer geared towards a variety of workers' compensation stakeholders, including clinically focused content, updates on current legislation and policy initiatives, education and recommendations for claims professionals on helping to identify and mitigate safety and cost issues within claims, and general awareness of trending cost drivers in both pharmacy and ancillary benefits management.

I hope that the articles we include in this edition of *RxInformer* help provide the context you need to make decisions as they relate to your role in managing care for the injured worker.

MED MONITOR

WORKERS' COMPENSATION PROFESSIONALS SHOULD KEEP AN EYE ON THESE MEDICATIONS

The FDA announced a number of drug approvals in recent months that could potentially impact workers' compensation, with additional approvals pending in upcoming months. These include new products and/or indications, new dosages or formulations of existing products, and generics introduced to the market.

Sustiva® (efavirenz) tablets • *

For treatment of HIV type 1 infection

Zipsor® (diclofenac potassium) capsules •

PAIN

Relief of mild to moderate acute pain

Viekira Pak[™] (ombitasvir, paritaprevir, and ritonavir tablets; dasabuvir tablets) + *

ANTIVIRAL

New indication extending treatment without ribavirin to patients with hepatitis C genotype 1b, with or without compensated cirrhosis

Inflectra® (infliximab-dyyb) for injection + *

RHEUMATOID ARTHRITIS A biosimilar to Remicade®; for the treatment of patients with moderate to severe rheumatoid arthritis

Avandaryl® (rosiglitazone maleate and glimepiride) tablets ■

DIABETES

Adjunct to diet and exercise to improve glycemic control in adult type 2 diabetes

Crestor® (rosuvastatin calcium) tablets ■

CARDIOVASCULAR Treats a variety of cholesterol disorders

FEBRUARY

♦ NEW PRODUCT/INDICATION

- FIRST-TIME GENERIC
- ♦ NEW DOSAGE/FORMULATION
- * SPECIALTY

Odefsey® (emtricitabine/ rilpivirine/tenofovir alafenamide) + *

ANTIVIRAL

For treatment of HIV type 1 infection

Voltaren® (diclofenac sodium) topical gel 1% ■

PAIN

Provides relief of pain for osteoarthritis of joints amenable to topical treatment

Probuphine[®] (buprenorphine hydrochloride) subdermal implant + *

OPIOID DEPENDENCE Subdermal implant formulation of the partial opioid agonist buprenorphine, for maintenance treatment of opioid dependence

Exalgo® (hydromorphone HCI) extended-release tablets •

PAIN

Opioid agonist administered once daily to manage moderate to severe pain in patients requiring continuous, around-the-clock analgesia

Ofirmev® (acetaminophen) injection ■

PAIN

Treats mild to moderate pain, and can treat moderate to severe pain in conjunction with opioids

*The generic version of Ofirmev cannot be launched until December 6, 2020, unless special circumstances are met.

Epclusa® (sofosbuvir/ velpatasvir) tablets ◆ *

ANTIVIRAL

For the treatment of hepatitis C virus genotypes 1-6

Byvalson[™] (nebivolol and valsartan) tablets +

CARDIOVASCULAR
For treatment of hypertension to lower blood pressure

Fenoglide® (fenofibrate) tablets ■

CARDIOVASCULAR Treats a variety of cholesterol disorders

Troxyca® ER (oxycodone hydrochloride and naltrexone hydrochloride) extended-release capsules +

PAIN

Opioid agonist with abuse-deterrent properties indicated for pain severe enough to require daily, around-theclock, long-term opioid treatment for which alternative therapies are inadequate

Evzio® (naloxone hydrochloride) auto-injector ◆ ♦

OPIOID OVERDOSE
Used for the emergency
treatment of known or suspected
opioid overdose. Originally
available in 0.4 mg/mL dosage,
an NDA was approved for a
more concentrated 2 mg dosage

AUGUST

T_____loctober

JULY

Adlyxin® (lixisenatide) injection +

DIABETES
Once-daily injection to improve

Once-daily injection to improve blood sugar control in adults with type 2 diabetes

Viekira XR™ (dasabuvir, ombitasvir, paritaprevir, and ritonavir) extendedrelease tablets • *

ANTIVIRAL

New extended-release tablets for certain patients with hepatitis C genotype 1a or 1b

Relistor® (methylnaltrexone bromide) tablets ♦

OPIOID SIDE EFFECTS New oral tablets to replace injections for the treatment of opioid-induced constipation (OIC)

SEPTEMBER

Invokamet® XR (canagliflozin/metformin hydrochloride) extendedrelease tablets +

DIABETES

Once-daily adjunct to diet and exercise to help control blood sugar levels in adults with type 2 diabetes mellitus

Amjevita[™] (adalimumabatto) injection **+** *

RHEUMATOID ARTHRITIS A biosimilar to Humira®; for the treatment of multiple inflammatory diseases, including severe rheumatoid arthritis

Ziagen® (abacavir sulfate) oral solution ■ *

ANTIVIRAL

Indicated for the treatment of HIV-1 infection, in combination with other antiretroviral agents

▶ ALWAYS ON THE WATCH

The new product landscape is evershifting. Visit MED MONITOR online for all of the latest updates, plus an expanded list of medications at healthesystems.com/rxinformer.

PRODUCTS ON THE HORIZON

The following product NDAs are under review by the FDA, and some may be approved in the near future.

Oliceridine (TRV130)

PAIN

Intravenous analgesic for moderate-to-severe acute pain with reduced frequency of opioid-related adverse events (e.g., nausea, vomiting, hyperventilation) when compared to intravenous morphine.

Arymo™ ER (morphine sulfate)

PAIN

Extended-release, potentially abuse-deterrent tablet formulation of morphine. Resistant to methods of manipulation, including injection and snorting, as well as oral abuse.

Vantrela[™] ER (hydrocodone bitartrate)

PAIN

Long-acting, extended-release opioid with abuse-deterrent properties, indicated for pain severe enough to require daily, around-the-clock, long-term treatment.

Naldemedine

OPIOID SIDE EFFECTS

Oral, peripherally acting mu-opioid receptor antagonist that treats opioid-induced constipation (OIC) in patients with chronic non-cancer pain.

Rapastinel (GLYX-13)

PSYCHIATRY

Intravenous formulation for the adjunctive treatment of major depressive disorder. Has been granted breakthrough therapy status.

CL-108

PAIN

Bi-layered tablet of immediate-release promethazine and modifiedrelease hydrocodone and acetaminophen, indicated for the relief of moderate to severe pain while preventing or reducing opioidinduced nausea and vomiting.





PROBUPHINE ENTERS THE MARKET

Subdermal Implant for Opioid Dependence Now Available

Probuphine® (buprenorphine hydrochloride), a subdermal implant for the maintenance treatment of opioid dependence in patients clinically stable on ≤8mg of transmucosal buprenorphine, is now available.

The implant consists of four one-inch rods inserted under the skin of the upper arm, providing low, steady doses of buprenorphine. Implantation requires a physician trained for the surgery, but many buprenorphine prescribers have little experience in surgery, nor the facilities to conduct surgery. Efforts to train physicians are underway.

AMITIZA LABEL REVISED

Update Made to List of Adverse Effects

The FDA recently approved a labeling revision for the chronic constipation drug, Amitiza[®] (lubiprostone), adding loss of consciousness and hypotension to the drug's list of adverse effects. Amitiza may appear in workers' compensation claims because opioids – commonly used to treat pain resulting from workplace injuries – are known to cause opioid-induced constipation (OIC), requiring further drug therapy. It is important that claims professionals understand the risks that come with Amitiza in the event a patient receives the drug for OIC.

BOXED WARNINGS ADDED TO OPIOIDS AND BENZODIAZEPINES

FDA Attempts to Prevent Deadly Combination

In an effort to decrease the combined use of opioids and benzodiazepines, the FDA added Boxed Warnings to the drug labeling of prescription opioids and benzodiazepines. Opioids are primarily used to treat pain, while benzodiazepines are primarily used to treat anxiety, insomnia, and seizures. FDA review found growing usage in the combination of these drugs, which can lead to slowed or difficult breathing and death. Opioids and benzodiazepines are commonly prescribed together in workers' comp, despite best practice recommendations.

CETYLEV RECALLED DUE TO INADEQUATE SEAL

Acetaminophen Overdose Antidote Recalled

Cetylev® (acetylcysteine) effervescent tablets for oral solution, an antidote for acetaminophen overdose, has been voluntarily recalled by Arbor Pharmaceuticals due to an inadequate seal of the blister pack. The improper seal of the product can lead to excess moisture and partial dissolution of the tablets, resulting in a potentially sub-therapeutic dose that could lead to risk of liver injury as well as possible microbial contamination. The recall impacts three lots of 500 mg strength Cetylev (Lot Numbers 005C16, 006C16 and 007C16, expiration date 02/2018) with NDC 24338-700-10.

Cannabis Conundrums: Making Sense of Tangled Marijuana Legislation

FAST FOCUS

The U.S. Drug Enforcement Administration (DEA) announced their decision this summer to uphold marijuana's status as an illegal Schedule I substance, but growing state momentum for the medical use of marijuana has resulted in diverse regulations. The fundamental differences between state and federal policies make it challenging to ascertain the future of medical marijuana in workers' compensation.

There has been much discussion regarding the use of medical marijuana in workers' comp as an alternative therapy for certain medical conditions, including pain. Insurance companies in Minnesota, Maine, and Connecticut have issued reimbursements to injured worker claimants for medical marijuana, and in 2015, the New Mexico Supreme Court ruled in favor of reimbursing medical marijuana in workers' comp claims.

Currently, 25 states and D.C. allow for the comprehensive use of medical marijuana, 5 but conflicts between federal and state regulation, as well as differences between states themselves, will make the management of medical marijuana difficult should it continue to permeate into workers' compensation.

DIFFERENCES IN EXISTING STATE LEGISLATION



Qualifying Conditions

What medical conditions make a patient eligible for medical marijuana?

Most states that have legalized medical marijuana allow it to be used for the treatment of chronic pain, seizures, muscle spasms, and cancer, but some states include additional conditions like arthritis and post-traumatic stress disorder (PTSD). Furthermore, states such as California and Massachusetts allow physicians to recommend the drug for medical conditions as they see fit, and Maine and Ohio allow the public to petition for more conditions to be added to their state's list of qualifying conditions.



Dosing and Days' Supply

How much marijuana should a patient receive?

Connecticut is one of many states that sets a limit on how much marijuana a patient can possess (2.5 ounces of marijuana every 30 days), but states like Pennsylvania and Maryland use the more abstract language of "a 30-day supply," which does not specify an amount. Meanwhile, Minnesota requires that patients discuss their condition and medical history with a pharmacist who then decides dosing and formulation. Several states allow for the home cultivation of medical marijuana (with varying limits to how many plants a patient can grow), where the patient is virtually self-dosing.



Formulations and Route of Administration

In what form will medical marijuana be given, and how will that affect the patient?

New York, Minnesota, Pennsylvania, and Ohio forbid the smoking of marijuana, and New York also bans edibles. Home cultivation in some states leaves administration up to the patient, but most states allow for vapors, smoking, tablets, tinctures, and liquids. Different routes of administration are just one variable that can impact the medicinal effects of marijuana in a patient, making it difficult to predict effectiveness.



Drug Sourcing

Where will patients' marijuana come from?

Medical marijuana is primarily obtained through dispensaries, but in states like Ohio, marijuana can only be dispensed by a pharmacist in a retail store. Home cultivation raises issues of drug sourcing, and states vary on the level of quality assurance that medical marijuana must undergo.



Pricing and Reimbursement

How much will marijuana cost, and how is that processed?

Marijuana is paid for in cash since it is illegal for a federally-related banking system to process funds related to the sale of a federally illegal substance. Therefore, even in a scenario where medical marijuana is clinically acceptable, it cannot go through the same adjudication process as prescription drug therapies. Instead, the claimant must pay out-of-pocket and be retroactively reimbursed by the insurer. This removes the insurer's ability to implement prior authorization protocols and other prospective strategies to manage the appropriateness and cost of therapy.

There is also limited visibility into marijuana pricing overall, making it difficult to determine appropriate cost benchmarks. Very few states have built-in measures to monitor pricing. New York, for example, requires dispensaries to divulge the costs of manufacturing, marketing and distribution to determine if prices are reasonable.



Workers' Rights

How will workers under the influence of medical marijuana be treated in the work environment?

Many states, such as Ohio and Colorado, allow employers to terminate employees under the influence of medical marijuana, or who test positive in random drug screenings and post-injury drugs tests, in order to promote workplace safety. Some states can deny workers' comp to those injured on the job if they are taking medical marijuana. However, states like Arizona and Minnesota have protective clauses in their legislation.



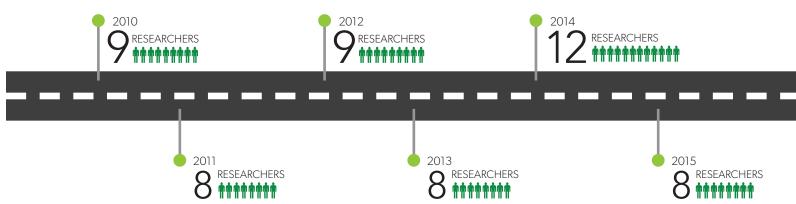
Research Roadblocks

The lack of evidence-based guidelines regarding the clinical management of medical marijuana further adds to the complexity of how this drug might fit into workers' comp. Research restrictions surrounding marijuana have limited the scope of scientific knowledge that could inform such guidelines. To date, no large-scale randomized controlled human trials have been conducted in the United States that sufficiently establish the benefits and risks of marijuana use.

Historically, only research institutions that have completed an intensive, time-consuming application process that involves the Drug Enforcement Administration (DEA), the National Institute on Drug Abuse (NIDA) and the U.S. Food and Drug Administration (FDA) have been allowed to study marijuana.⁶

Many researchers do not have the time or resources to complete the application, and the DEA verifies that the majority of applications received do not fulfill application requirements.

Researchers Who Received Marijuana From NIDA:6



With limited clinical insight available, physicians are often uncomfortable recommending medical marijuana because they do not know how it will impact the patient, or the specific role it may play in managing pain in the injured worker. When marijuana is recommended, it is often done so as a last resort when traditional therapies have failed and the potential benefits appear to outweigh the risks.

However, steps towards progress in clinical research are being undertaken.

Planting Seeds

Although the DEA recently announced their decision to uphold marijuana's status as a Schedule I substance, they did update their policy to expand marijuana research. Previously, only institutional researchers could study marijuana, but now private entities, upon successfully completing the application process, can become DEA-registered to grow marijuana for strictly commercial endeavors funded by the private sector and aimed at drug product development. This means that pharmaceutical manufacturers in the United States can now conduct research.

The pharmaceutical industry likely has more resources that could be devoted to completing the application process than an institutional research team, and this may foster greater scientific knowledge surrounding marijuana, potentially informing best practices and policies. However, it is unclear to what extent the pharmaceutical

industry will carry out such research, especially as the profitability of medical marijuana is yet to be fully determined when compared to existing therapies. In the case of pain management drugs, it is unknown whether medical marijuana would be profitable for pharmaceutical companies to pursue when compared to traditional pain management drugs, such as opioids.

Regardless, because any new research initiatives will take a great amount of time, we are likely to stay within the current paradigm for the foreseeable future.

Reaping What We Sow

Planning today for the future of medical marijuana is critical for industry leaders. Although the DEA has decided not to reschedule marijuana at this time, they did announce that they may reconsider such a decision at a future date. In the meantime, there is individual state policy to consider. In the presence of so much new and impending legislation, eventually the workers' comp industry must have the agility to incorporate medical marijuana protocols into existing claims management infrastructures.

Determining best practices will require significant education and input from all stakeholders as the status quo continues to evolve. There are many questions yet to be answered from clinical, policy, and workplace perspectives.



FAST FOCUS I

Trends show that women may face increased drug therapy risks with certain medications that are often prescribed within workers' comp. While these trends may be associated with biology, they can also be traced to social behaviors such as gender-biased clinical research and prescribing differences between women and men. Awareness of these risks and their causes is critical to understanding the specific needs and considerations of injured worker populations.

When we think of injured workers, we often think of men in casts and crutches who were hurt in labor-intensive jobs related to construction, machinery or heavy lifting. This imagery, while very much a real part of workers' comp, can dominate the minds of many and overshadow the significant portion of women in the injured worker population.

Women make up almost half of the workforce, and approximately 40% of nonfatal occupational injuries involve women. Women face many of the same risks for workplace injury as men, but when it comes to drug therapy, there exist certain gender-specific trends.

OPIOIDS

BENZODIAZEPINES

ANTIDEPRESSANTS

RELEVANCE TO WORKERS' COMP

Commonly used in workers' comp to manage pain from work-related injuries, opioids come with many inherent risks, as well as some gender-specific concerns.

Benzodiazepines are often prescribed in workers' comp for anxiety, muscle spasms, insomnia, and other concerns. Injured workers taking prescription opioids may experience side effects such as insomnia and anxiety, which can lead to the prescribing of benzodiazepines.

Injured workers who experience reduced function can develop depression, which can hinder their ability to recover and require the prescription of antidepressants.

EXAMPLES

Oxycodone Hydrocodone Codeine

Tramadol

Alprazolam Diazepam Lorazepam

Escitalopram
Fluoxetine
Sertraline
Citalopram
Duloxetine

RISKS

All patients, male and female alike, face significant risks when it comes to opioids, but gender-specific trends demonstrate that women may be more susceptible.

Women are more likely to be prescribed prescription pain medications such as opioids – often at higher doses and for longer durations – than men.³ Women are more likely to experience chronic pain,³ and they are more likely to use opioid analgesics than men.⁴

Every three minutes, a woman visits the emergency department due to prescription pain medications such as opioids, and deaths from prescription pain medications have increased more than 400% for women since 1999, compared to 265% among men.³ Women most susceptible to prescription pain medication misuse or abuse are between the ages of 25-54, an age that greatly represents the working population.³

To compound the problem, opioids are frequently prescribed along with benzodiazepines, despite serious, even lifethreatening risks of doing so.

The Centers for Disease Control and Prevention (CDC) warns against combining benzodiazepines and prescription pain medications, but benzodiazepines are almost always prescribed in combination with opioids in workers' comp, despite significant risks. The rate of overdose deaths involving benzodiazepines (not specific to gender) has quadrupled since 1996. Benzodiazepines are involved in 31% of opioid overdose deaths, and overdoses that involve benzodiazepines are 75% likely to involve opioids.

While the combination of opioids and benzodiazepines is a concern for any patient regardless of gender, the use of benzodiazepines is twice as prevalent in women than men. Benzodiazepines also send more women than men to emergency departments, and therefore trends involving benzodiazepines are incredibly relevant when considering potential drug therapy risks for this given patient population.

Women are twice as likely to be diagnosed with depression than men,¹⁰ they receive more antidepressants than men,¹¹ and they are more than twice as likely to take antidepressants prescribed to them than men.¹²

The CDC advises caution when combining antidepressants with prescription pain medications such as opioids.³ Women are more likely to visit an emergency department due to antidepressant use than men, and more women than men die from overdoses of antidepressants.³

WHY MIGHT WOMEN FACE INCREASED DRUG THERAPY RISKS?



Behavioral Differences

Women are more likely than men to seek the care of a physician, ¹³ making them less likely to neglect or ignore an injury or illness, and more likely to be prescribed drug therapy. In general, women are significantly more likely to use a prescription drug to manage health concerns than men, ¹⁴ and women are more likely to engage in doctor shopping – the obtaining of prescriptions from multiple prescribers – than men.³



Biological Differences

One thing we must remember is that women and men have several biological differences, ranging from hormonal differences to dimensional differences in organs. Women may react differently to certain drug therapies, and they may exhibit different symptoms than men

For example, research has shown that women experience more intense opioid cravings than men,¹⁵ and they become dependent on prescription pain medications more quickly than men.³ Women are also nearly twice as likely to experience adverse drug reactions overall.¹⁶ However, it is possible these risks stem from gender bias in medical research due to the fact that the female experience is not studied in enough depth.



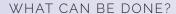
Social Differences

Women are underrepresented in clinical trials, and there is no law or official policy that requires the inclusion of women in industry-sponsored clinical trials.¹⁶

A lack of research, inclusion, and awareness leads to gaps in medical care. Interventions and testing may be tailored to the needs of men, leaving women with care that does not adequately meet their specific needs. For example, while clinical trials for depression treatments do include women, the trials may not examine outcomes by gender, and women and men may differ in response to depression treatment.¹⁷ Not taking such differences into consideration could lead to suboptimal care.

Furthermore, trends indicate that physicians exhibit different prescribing patterns when it comes to women and men. As noted earlier, physicians are more likely to prescribe women prescription pain medications such as opioids, as well as drugs such as benzodiazepines and antidepressants.

If women are not receiving care that is appropriate for their specific needs, their condition could worsen or complicate, or they may experience new or exacerbated adverse events. Ultimately, this results in poor injured worker outcomes. From a payer perspective, this prolongs the life of the claim and leads to higher medical costs.



Injured female workers benefit greatly when drug therapy adheres to evidence-based guidelines – particularly when it comes to potentially dangerous and addictive medications such as opioids and benzodiazepines. Mood-altering drugs such as antidepressants and antianxiety medications also warrant a closer look into the patient profile to determine if psychosocial concerns could be interfering with recovery, as depression and anxiety are often associated with opioid misuse.¹⁸

But superior claims management requires looking beyond drug therapies and towards the patient receiving them. Characteristics such as gender should be considered when managing a patient as those characteristics may have related trends and impacts. Patient characteristics are part of a holistic picture of health that can highlight intervention opportunities.

GENDER CONSIDERATIONS IN WORKERS' COMPENSATION

Women make up half the workforce¹ and ~40% of nonfatal occupational injuries,² comprising a significant portion of the injured worker population. However, there is a lack of awareness surrounding the social and biological differences between men and women as they relate to drug therapy risks. These gender-specific trends should be considered when managing drug therapy in injured female workers.

OPIOIDS

TRENDS

Research shows that women are more likely than men to:

Experience opioid cravings³



Be prescribed pain medications, including opioids, often at higher doses and for longer durations⁴

IMPACTS4

18 women die every day from prescription pain medication overdoses

Deaths from prescription pain medication overdoses have **increased 400%** for women since 1999 For every woman that dies from pain medication overdose, **30 visit the emergency department** for misuse or abuse.
That's one every 3 minutes



REFERENCES: 1. Women's Bureau, U.S. Department of Labor. American women: looking back, moving ahead: the 50th anniversary of the president's commission on the status of women report. March 2015. 2. Bureau of Labor Statistics. Nonfatal occupational injuries and illnesses requiring days away from work, 2013 [news release]. December 2014. 3. Back SE et al. Am J Drug Abuse. 2011;37(5):313-23. 4. CDC. Vital Signs: Prescription Painkiller Overdoses. July 2013. http://www.cdc.gov/vitalsigns/prescriptionpainkilleroverdoses/index.html. 5. Olfson M et al. JAMA Psychiatry. 2015;72(2):136-142. 6. Bachhuber MA et al. Am J Public Health. 2016;106:686-8. 7. CDC. Vital Signs: Variation Among States in Prescribing of Opioid Pain Relievers and Benzodiazepines — United States, 2012. July 2014. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6326a2.htm 8. Mayo Clinic. Depression in women: Understanding the gender gap. http://www.mayoclinic.org/diseases-conditions/depression/in-depth/depression/art-20047725. Published January 2016. 9. Pratt LA et al. Antidepressant use in persons aged 12 and over: United States, 2005–2008. NCHS data brief, no 76. National Center for Health Statistics. October 2011. http://www.cdc.gov/nchs/products/databriefs/db76.htm 10. Arteta J et al. Pain Med. August 2015. doi: 10.1111/pme.12886.

BENZODIAZEPINES



TRENDS

Benzodiazepine use is 2xmore prevalent in women⁵

Frequently prescribed with opioids despite severe risks

IMPACTS

Send more women than men to emergency departments4

The rate of overdose deaths quadrupled from 1996-20136 Involved in 31% of opioid overdose deaths7



ANTIDEPRESSANTS

AWARENESS & BEST PRACTICES

These gender-specific trends and impacts must be considered when managing a patient's claim. Gender is one of many characteristics that paint a holistic picture of a patient's health, and these differences could highlight opportunities for intervention. These concerns further illustrate why conservative, evidence-based guidelines should be practiced to reduce risks in drug therapy.

TRENDS



Women are:

2x more likely to be diagnosed with depression 2.5x more likely to take antidepressants than men⁹

IMPACTS

Depression can delay recovery and increase the likelihood of prescription opioid abuse¹⁰

Women are more likely to visit an emergency department due to antidepressants4

More women than men die of overdoses from antidepressants4



THINKING OUTSIDE THE CLAIM



FAST FOCUS:

Development of a predictive model that incorporates multidimensional data can enable us to better anticipate the treatment needs, considerations and challenges of specific patient populations – enhancing our ability to monitor and intervene in a claim with unprecedented insight.

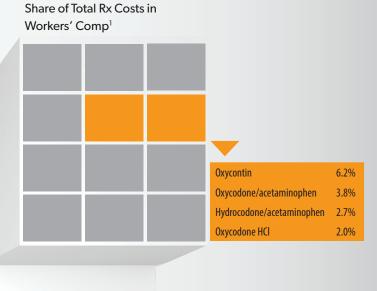
Understanding population data can help payers better understand the specific treatment needs and potential challenges of patients within a population (see "How to Treat a Lady: Drug Therapy Risks for Women in Workers' Comp"

on page 15). But acknowledging these data only scrapes the surface of possibilities. The natural evolution is to then synthesize and construct data in a way that not only helps illuminate these needs and challenges, but enables us to anticipate them before they occur.

Gathering and analyzing large-scale, multidimensional data over a period of time lends itself to the construction of a predictive model on which patient management decisions can be made that impact future outcomes.

GETTING AHEAD OF OPIOIDS

One example of how population data can be used to impact future claims outcomes in a significant way is by the identifying the risk for potential opioid misuse. Considering four of the top ten drugs in workers' compensation are opioid products comprising 15% of total pharmacy spend, getting out in front of opioids would serve to dramatically impact the cost of a claim as well as the overall health of the injured worker.



Top 4 opioids
comprise
15% of total
Rx costs

MULTIDIMENSIONAL VIEW OF RISK

There already exists a number of established risk factors that prescribers should consider when weighing the risks and benefits of opioid medication in a particular patient – two examples being a history of substance use disorder and the presence of psychosocial factors. Although certain risk factors associated with drug misuse have been studied, few published studies have used data from a wide variety of multidimensional sources such as occupation, employer types, lifestyle preferences, and other non-pharmacy information to develop models that identify patients at risk for prescription opioid misuse.

Taking a more inclusive, multidimensional view of patient data can help payers go beyond considering the most basic risk factors to truly understand the unique risk profile of their particular claims populations. This enables payers to apply more than just basic intervention strategies, and to customize management to maximize the impact on claims outcomes.



Healthesystems analyzed 40,000 claims from the last five years to develop a model that could help estimate potential opioid misuse within a given population.² Misuse in this model was defined as a morphine equivalent dose (MED) higher than the recommended amount.

Because the goal was to identify a more comprehensive set of potential risk factors for opioid misuse, a variety of data types were included in the analysis that may not typically factor into medication management.

Examples of Data Types Analyzed in a Predictive Model







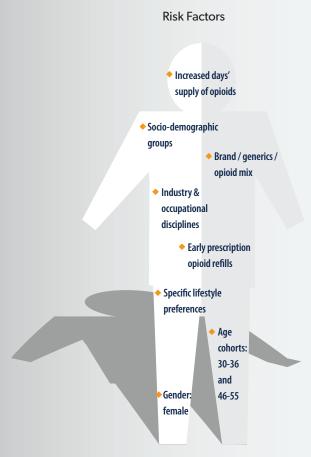






THINKING OUTSIDE THE CLAIM

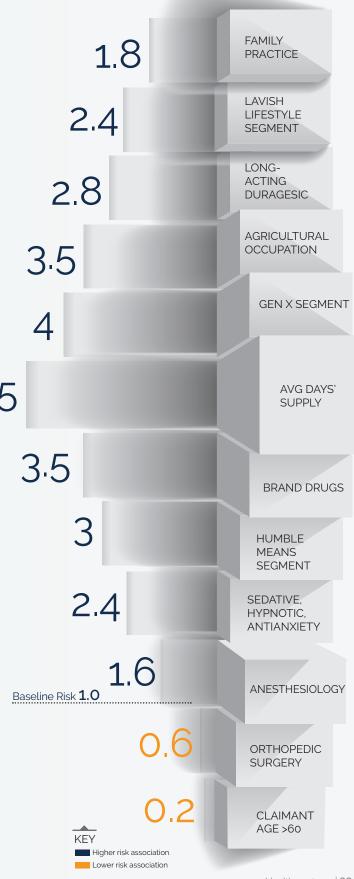
Although some of the factors significantly associated with prescription opioid misuse were expected (e.g., increased days' supply, early refill patterns), a number of risk factors emerged that have a less-than-obvious association with potential misuse. And importantly, some of these risk factors – such as socioeconomics and lifestyle preferences – are information that isn't readily visible within a claim.



Once risk factors are identified, we can take it a step further and assign a specific level of risk to each factor to determine which ones are most likely to drive opioid misuse. For the drivers illustrated to the right, any value higher than 1.0 indicates increased risk for opioid misuse, and any value below 1.0 indicates a reduced risk for opioid misuse.

For example, a patient prescribed opioids by a family physician is at significantly higher risk than the patient prescribed opioids by an orthopedic surgeon. This could be due to a number of factors, including differences in setting (e.g., opioids are typically appropriate for a short-term, post-operative setting), timing (a patient may be under the care of a family physician versus a specialist at different points in the care continuum), or expertise (a primary care physician may not be as well-versed in the management of opioid medications versus a specialist in the field). Despite the reasons, the driver itself is an important insight given that primary care physicians are the top prescribers of pain medications in the United States.³

Drivers of Opioid Misuse and Their Varying Levels of Risk



WHAT MEDICATION MIX REVEALS

While the findings reinforce our need to look at new and more varied aspects of patient data, a predictive model can also enhance our ability to gain insight into a claim's risk level based on drug mix.

A second analysis uncovered prescription patterns that exist between high-risk and low-risk opioid patients. Claims containing a more complex medication mix were more likely to see an increase in MED. The basic connections that typify these claims are some iteration of the following:

Hydrocodone/acetaminophen is typically the central component of medication regimens in the opioid claim population



Analytics that consistently demonstrate risk correlation between a specific drug or drug mix can provide much-needed support to guide clinical decision-making in a way that can effectively reduce or even prevent patient risk. As noted earlier, hydrocodone/acetaminophen is one of the most commonly prescribed drugs in workers' compensation, and the nation's most popular pain medication. According to the DEA, hydrocodone is also the most abused prescription opioid in the United States. The presence of hydrocodone/acetaminophen as the cornerstone for medication regimens among high-risk opioid claims reinforces the concern that prescribers may underestimate its risks in leading to elevated MED, misuse, and chronic opioid use and dependence.

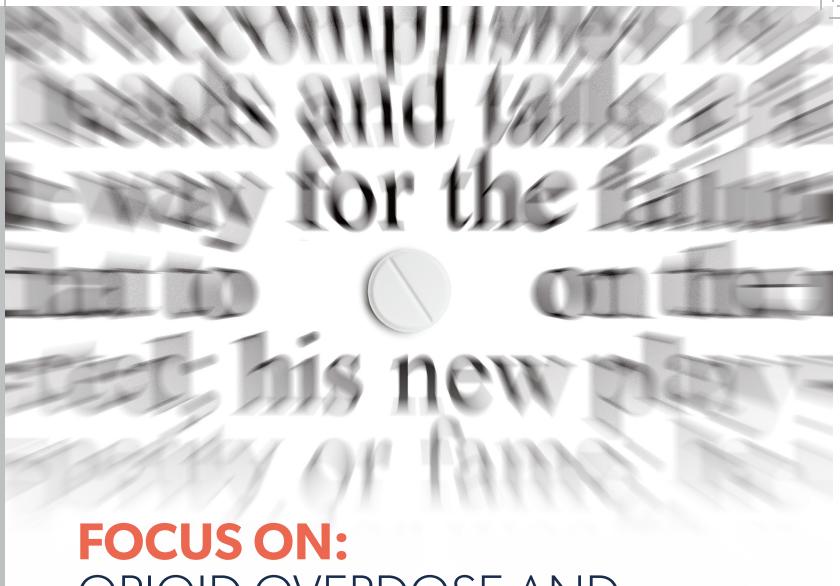
Analytics that consistently demonstrate risk correlation between a specific drug or drug mix can provide much-needed support to guide clinical decision-making in a way that can effectively reduce or even prevent patient risk.

CURRENT AND FUTURE APPLICATION

The results uncovered reinforce the continued importance of identifying and managing new and potentially overlooked therapy risks, and the need to look more deeply and more comprehensively at patient data. Using pharmacy drug, demographics, employer, and medical claims data, it is feasible to develop predictive models that could assist prescription monitoring programs, payers, and healthcare providers in evaluating patient characteristics associated with elevated risk for prescription opioid misuse.⁴



The data included in this article originally appeared in the poster Estimating Potential Misuse of Prescription Opioids by Injured Workers in Workers' Compensation, presented at the American Academy of Pain Medicine (AAPM) 2016 Annual Meeting by Healthesystems Chief Medical Officer, Robert Goldberg, MD, FACOEM.



OPIOID OVERDOSE AND DEPENDENCE THERAPIES

FAST FOCUS

State and federal legislation have increasingly embraced the use of naloxone to treat opioid overdose, as well as drugs that treat opioid dependence, particularly buprenorphine. But when should these products be prescribed, and what do they signify when present in a patient's profile?

There have been many developments in the fight against opioids, including the expansion of access to drugs that combat opioid dependence and overdose. Claims professionals could see these medications appear more frequently in patient profiles, especially as state and federal legislation make these drugs more readily available. It is important that claims professionals

understand the appropriate use of these drugs, as well as the reasons for use in certain patient populations, the differences between formulations, and appropriate precautions to consider when these drugs are prescribed to patients.

NALOXONE - THE OPIOID OVERDOSE ANTIDOTE

Naloxone blocks or reverses the effects of opioids and is used to counteract an opioid overdose. The presence of naloxone in a patient's profile is concerning and warrants a closer look into the patient's current opioid therapy. However, naloxone may be prescribed for various reasons.

Naloxone Formulations

Commercially, naloxone is available as Evzio® auto-injector and Narcan® nasal spray. Both products consist of naloxone hydrochloride and work within minutes of administration.

Embracing Naloxone

Congress passed the Comprehensive Addiction and Recovery Act (CARA), raising hundreds of millions of dollars to expand treatment for opioid addiction and overdose. CARA will award grants up to \$200,000 to eligible entities to expand access to naloxone, with \$5 million approved for these grants every year from 2017 to 2021.¹

Forty-seven state governments have also passed various laws that expand layperson access to naloxone, making it easier for medical professionals to prescribe and dispense naloxone, and encouraging laypersons to administer naloxone without fear of legal repercussions.² Meanwhile, 36 states encourage Good Samaritans to summon aid in the event of an overdose.²

Furthermore the Centers for Disease Control and Prevention (CDC) recommends co-prescribing naloxone along with opioid therapies 50 MME/day or higher,³ which could lead to physicians prescribing naloxone more frequently.

Reasons Naloxone May Be Prescribed to a Patient

- Opioid therapy is 50 MME/day or higher (per CDC recommendations)
- Patients may be on rotating opioid regimens⁴
- Patients may be taking extended-release or long-acting opioids⁴
- Patients may be undergoing detox or opioid abstinence, which can lower a patient's opioid tolerance, thereby making them susceptible to overdose⁴
- Patients may have comorbidities such as chronic obstructive pulmonary disease (COPD), asthma, sleep apnea, and other breathing disorders that increase the odds of respiratory depression

Considerations When Oddressing Naloxone in a Patient's Profile

- Look into the patient's current opioid therapy regimen.
- Verify if best practices, including medication agreements, pill counts, and urine analysis have been documented regarding the patient's opioid therapy
- Determine if naloxone was prescribed due to a best-practice recommendation
- Look for comorbidities
- Examine the prescriber's prescribing patterns
- Contact appropriate stakeholders such as the prescriber(s), the patient, and the case manager
- Look for any refills of naloxone products
- Understand cost differences between naloxone-containing products. Evzio has increased dramatically while Narcan has remained relatively steady in comparison

THE CDC RECOMMENDS CO-PRESCRIBING NALOXONE ALONG WITH OPIOID THERAPIES 50 MME/DAY OR HIGHER

BUPRENORPHINE FOR OPIOID DEPENDENCE THERAPY

Treating Opioid Dependence vs Pain

Buprenorphine is a partial opioid agonist indicated for the treatment of opioid dependence. Buprenorphine helps to reduce opioid withdrawal, but there are also formulations of buprenorphine indicated to treat pain, and it is important to ensure that buprenorphine products are prescribed for their respective FDA-approved indication.

Regardless of the indication, buprenorphine can produce euphoria and respiratory depression, though it is not as potent as full opioid agonists.⁵ Similar to full opioid agonists, buprenorphine can be abused, misused, and diverted. In Massachusetts prisons, buprenorphine accounted for 12% of contraband.⁶

Embracing Buprenorphine for Opioid Dependence

The Department of Health and Human Services (HHS) allowed medical practitioners with special waivers to prescribe buprenorphine to up to 100 patients for a year or more, and a recent rule update now increases that limit to 275 patients.⁷ As this rule allows prescribers to treat more patients, the prevalence of buprenorphine may increase in workers' compensation.

Furthermore, CARA now allows nurse practitioners and physician assistants to prescribe drugs, such as buprenorphine, for medication-assisted treatment of opioid dependence. Not only does this increase the number of people who can prescribe buprenorphine, but CARA will also allocate \$5 million a year to expand the use of medication-assisted treatments for opioid dependence, which includes buprenorphine, from 2017 to 2021.

BUPRENORPHINE PRODUCTS FOR THE TREATMENT OF OPIOID DEPENDENCE

The following medications are FDA-approved for the treatment of opioid dependence and should not be used for the treatment of pain:



Subutex® is the first buprenorphine formulation for the treatment of opioid dependence; there are many generics available, though Subutex is primarily for patients who cannot receive naloxone, an opioid antagonist included in most modern formulations to deter abuse, due to intolerance, allergies, and possible drug-drug interactions if the patient is on another medication



Suboxone[®] (buprenorphine and naloxone) is available as both a sublingual tablet and a sublingual film. Generics are only available for the tablets, though the film dissolves quicker, which may help with medication adherence efficacy



Bunavail® (buprenorphine and naloxone) is a buccal film more efficient than suboxone, allowing lower doses of buprenorphine to achieve similar effects. The lower dosage levels decrease the potential for side effects, but no generics are currently available



Zubsolv® (buprenorphine and naloxone) is a sublingual tablet also more efficient than suboxone. Zubsolv dissolves in seconds, quicker than other products, with a mint flavoring that patients may find easier to tolerate. No generics are currently available



Probuphine® (buprenorphine hydrochloride) is a subdermal implant of four one-inch rods placed under the skin of the upper arm, providing low, steady doses of buprenorphine for six months. Probuphine is a novel drug meant for patients currently stable on 8 mg or less of transmucosal buprenorphine. It is not a first-line treatment and requires special surgery, which may be difficult to facilitate, though it reduces the burden of medication adherence

Buprenorphine Products for the Treatment of Pain

The following medications are FDA-approved for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment for which alternatives treatments are inadequate:

- ▶ Belbuca™ (buprenorphine hydrochloride) is a long-acting buccal film that adheres to the inside of the cheek and dissolves within 30 minutes. This drug was approved October 2015, meaning no generics will be available in the near future
- BuTrans® (buprenorphine) transdermal system is a onceweekly topical patch. No generics are currently available, though the drug's exclusivity status has expired, meaning generics could arrive in the future

Dependence Products Should Not Be Used to Treat Pain

In workers' compensation, buprenorphine products only approved to treat opioid dependence are often prescribed off-label to treat pain, despite the fact that there is no peer-reviewed published data or clinical practice guidelines on how to safely do so.⁸ Patients who need treatment for pain but not addiction should be treated within the context of traditional drug therapy with FDA-approved agents for pain. Such drug therapy should also be carried out for a well-monitored duration based on treatment guidelines.

Considerations When Oddressing Buprenorphine in a Patient's Profile

- Become familiar with different buprenorphine products
- Verify that buprenorphine products are prescribed for their respective FDQ-approved indications
- In claims where buprenorphine has been prescribed for opioid dependence, check to see that psychosocial therapy has also been included
- Look for signs of opioid abuse, misuse, and diversion

Pharmacy Management – Don't Overlook the Impact of Age and Comorbidity

By Silvia Sacalis, PharmD, VP of Clinical Services, Healthesystems

The presence of comorbid conditions within a workers' compensation claim can impact pharmacy management in ways that go beyond the obvious. Superior pharmacy management requires looking not only at drug therapies, but also considering the various characteristics of the patient who is receiving them.

Claims with a comorbidity have been steadily increasing over the last decade, contributing to increases in overall medical costs. In general, comorbidities add to the complexity of a claim as more drug therapies are added to manage multiple conditions, in addition to the medications treating the work-sustained injury or illness. This leads to polypharmacy and a greater potential for drug-drug or drug-disease interactions. It can also mean the presence of multiple prescribers to manage different conditions, making it impossible for any one physician to manage a patient's complete treatment plan.

But certain comorbidities bring some unique considerations to pharmacy management in the injured worker. The following are some examples of note:

RESPIRATORY DISORDERS
Examples of respiratory comorbidities include chronic obstructive pulmonary disease (COPD), asthma, sleep apnea, and other breathing disorders.

Increased risk for opioid events:

Respiratory depression is a significant and potentially fatal adverse event of opioids. Injured workers with a respiratory disorder face increased risk of respiratory depression.

Certain opioids such as oxycodone are contraindicated in patients with specific respiratory conditions, and guidelines recommend that opioid therapy should be avoided in patients with sleep-disordered breathing, including sleep apnea.²

Naloxone prescribing: Should a prescriber choose to prescribe an opioid therapy to a patient with a respiratory disorder, they may also prescribe the opioid overdose reversal agent naloxone as a precautionary measure. PSYCHOSOCIAL DISORDERS
Psychosocial disorders such as depression and anxiety are prevalent within the injured worker population. These disorders can predispose an injured worker to chronic pain, impede recovery and return to work, and increase the potential for opioid misuse³; thus it is important to address and treat psychosocial comorbidities. But psychotropic drugs used to treat these disorders can introduce their own risks.

Psychotropic drug misuse:

Benzodiazepines, commonly prescribed in workers' compensation to treat anxiety, are a frequently misused drug class. Antidepressant misuse, while not as common, does contribute to overdoses and emergency department visits, especially in women.⁴



ADVANCED AGE

The aging workforce continues to have an increasing impact on the

management of workers' compensation claims populations. While age itself isn't necessarily a comorbidity, claimants with a comorbid condition are often older than other claimants and require some specific prescribing considerations.1

Increased polypharmacy risk:

Older patients are more likely to be prescribed multiple prescriptions for long-term durations. A large portion of older adults also use over-the-counter medications and dietary supplements, which aren't visible within a workers' comp claim. These scenarios increase the risk that polypharmacy may occur - or even go unnoticed.

- **Increased side effects:** A number of drugs are contraindicated in the older population due to increased propensity for side effects. Other drugs may require special considerations or dosage adjustments to reduce potential side effects. For example, non-steroidal anti-inflammatory drugs (NSAIDs) prescribed to manage pain present an increased risk for stomach ulcers in patients age 60 or older. Thus concomitant prescribing of a gastroprotective medication may be appropriate.
- Drug metabolism changes: A medication dosing schedule for a patient who is 30 years old may not be appropriate for a patient who is 50 years old due to changes in drug metabolism that occur as a person
- Cognitive decline: Older patients may experience cognitive decline, which could lead to forgetting to take medications (nonadherence), taking medications too often (misuse), or irregular refill trends.



HYPERTENSION

Hypertension (high blood pressure) is the most prevalent comorbidity among claims

examined by the National Council on Compensation Insurance (NCCI).1

NSAID-related events:

NSAIDs prescribed to manage pain in injured workers (e.g., naproxen, ibuprofen) can cause blood pressure to rise even higher, putting greater stress on the heart and kidneys.

Antidepressants:

Certain antidepressant medications commonly prescribed to treat psychosocial disorders in injured workers (e.g., fluoxetine, venlafaxine) can also raise blood pressure, increasing risk of a cardiovascular event.

Erectile dysfunction medications: Tadalafil is among commonly prescribed medications in workers' compensation, typically to treat opioid-induced erectile dysfunction. It too can contribute to high blood pressure.



SUBSTANCE ABUSE DISORDER A history of substance abuse,

including prescription medications, illicit drugs, or alcohol, is the number one red flag for potential opioid abuse. However, there are other considerations beyond opioids when determining appropriate pain management strategies for these patients.

Other prescription drug misuse:

A history of substance abuse can predispose an injured worker to prescription drug misuse. Commonly prescribed medication classes within workers' compensation have increased potential for misuse, including benzodiazepines (e.g., diazepam, alprazolam) and sleep aids (e.g., zolpidem, eszopiclone).

Acetaminophen toxicity:

Because pain management options are limited in patients with a history of substance abuse, prescribers may turn to alternative medications such as acetaminophen. An important factor for consideration prior to prescribing acetaminophen in patients with a history of alcohol abuse is that they may have a compromised liver, putting them at increased risk for acetaminophen toxicity.

Naloxone prescribing:

If opioids are prescribed in patients with a history of substance abuse, the Centers for Disease Control and Prevention (CDC) recommend that the opioid overdose reversal agent naloxone be prescribed concomitantly.2



ABOUT Silvia Sacalis, PharmD

Silvia Sacalis, PharmD, provides clinical leadership as Vice President of Clinical Services at Healthesystems. Her experience and clinical expertise span the PBM, retail pharmacy and managed care environments. Leveraging her technology background, clinical skills and management expertise, she helps develop and operationalize strategic clinical initiatives to help workers' compensation insurance payers maximize the impact of a pharmacy benefit management program. Throughout her career, she has held various leadership roles

in which she provided oversight of the development of clinical services programs, and integration of analytics technology with clinical consultative support.



What Should Claims Professionals Know About **Therapeutic Duplication**?



A claims professional sees prescriptions for an oral nonsteroidal anti-inflammatory drug (NSAID) and a topical NSAID gel, both indicated for the patient's knee pain. Is it appropriate to approve the two NSAIDs concurrently?

Depending on various factors, this may be an example of therapeutic duplication.

WHAT IS THERAPEUTIC DUPLICATION?

Therapeutic duplication is the prescribing of multiple medications for the same indication. In an effort to reduce medication-related problems, promote patient safety, and reduce total claim costs, therapeutic duplication should be avoided.

WHAT ARE THE SAFETY CONCERNS OF THERAPEUTIC DUPLICATION?

Therapeutic duplication increases the likelihood that a patient can experience adverse effects due to increased ingredient concentrations in the body, as well as drug-drug interactions. This is potentially harmful to the patient and should be avoided.

For example, a patient with a high concentration of NSAIDs may experience:

- Stomach problems such as bleeding and ulcers (specific to oral NSAIDs)
- High blood pressure
- Heart problems
- Swelling of the lower legs, feet, ankles, and hands
- Kidney problems
- Rashes

COMMON NSAIDS INVOLVED IN THERAPEUTIC DUPLICATION INCLUDE:

Oral

- Ibuprofen
- Naproxen
- Celecoxib
- Meloxicam

Topicals

- Compounds containing NSAIDs
- Diclofenac 3% gel (Solaraze™)
- Diclofenac 1.5% solution (Pennsaid®)
- Diclofenac 2% solution (Pennsaid)
- Diclofenac 1.3% patch (Flector®)

WHAT ARE THE COSTS OF THERAPEUTIC DUPLICATION?

First and foremost, therapeutic duplication results in waste, but therapeutic duplication can also result in adverse effects, which may worsen a patient's health, requiring additional drug therapy or possible hospitalization, increasing the cost of the claim.

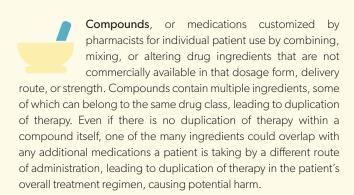
HOW DOES THERAPEUTIC DUPLICATION OCCUR?

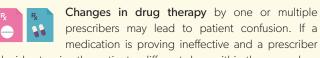
Therapeutic duplication is often seen in a claim, and it is imperative that claims professionals are aware of the various causes:



Polypharmacy, or the simultaneous use of multiple medications in an individual patient. A patient may be taking concurrent medications for a preexisting condition unrelated to their work injury, in addition

to medications for their injury. Furthermore, the medications they are taking for their injury could be causing side effects that require additional treatment. It is important to avoid risks associated with multiple medication use, such as therapeutic duplication, adverse effects, drug-drug interactions, drug-disease interactions, and inappropriate dosing.





decides to give the patient a different drug within the same drug class, the patient may inadvertently take the old drug in addition to the new drug, causing duplication of therapy.



Lack of communication between patients, prescribers, and other key stakeholders.

A patient may be taking over-the-counter medications, vitamins, herbals, homeopathic

products, or other prescription medications in addition to their injury-related medication, and this may not be communicated effectively between all relevant parties. A patient may also be visiting multiple prescribers who are unaware of the various drugs a patient is taking, and inadvertently prescribe drugs within the same class.



- ☐ Consider the timeframe were the drugs prescribed concurrently, or at different points in time?
- ☐ When in doubt, contact the prescriber to answer questions such as a potential change in therapy, or to establish medical need (e.g., oral NSAIDs during the day, an NSAID cream at night)
- ☐ Were the two drugs and/or formulations prescribed by the same prescriber, or multiple prescribers? Contact multiple prescribers to alert them of each other's involvement and of the patient's drug regimen
- ☐ In the event of therapeutic duplication where both products are clinically appropriate, consider selecting the most therapeutically appropriate and cost-effective product

MYTH: BUSTERS

PHYSICIAN DISPENSING EDITION

Some physicians argue that providing medications in-office benefits the patient. But the impact of this practice on workers' compensation patient outcomes – and ultimately costs – tells a very different story.

MUTH:

Physician dispensing improves patient adherence to medication, improving medical outcomes



Physician dispensing is associated with poorer clinical outcomes and more lost time

LOST TIME INCREASES WITH PHYSICIAN-DISPENSED DRUGS^{1,2}



MUTH:

Physician dispensing ensures closer patient monitoring, improving patient safety



Physician dispensing removes the safeguard of having licensed pharmacists act as a second line of defense to identify drug therapy risks such as:

- Drug-drug and drug-disease interactions
- Therapeutic duplication
- Inappropriate therapy or dosing



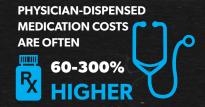
Vp to OF MEDICATION ERRORS HAPPEN AT PRESCRIBING³

MUTH:

Prices for physician-dispensed medications are equivalent to pharmacy-dispensed medications

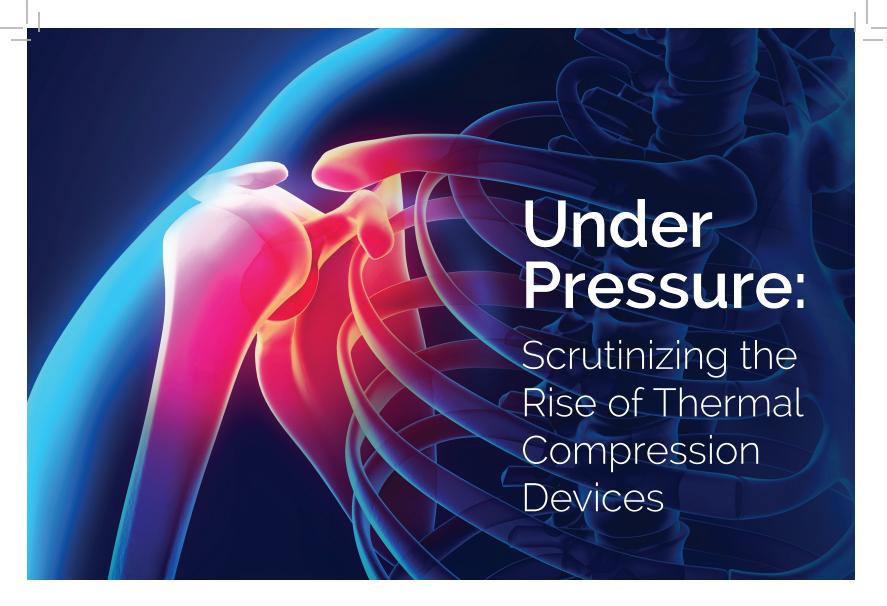


>90% of prescribers perceive their prices are equivalent to or lower than pharmacies.4 In reality, prices paid for physician-dispensed medications are often 60-300% higher for the same drugs dispensed by a retail pharmacy⁵



4 Reasons to Implement an Aggressive Physician-Dispensing Management Solution

- REDUCE PATIENT SAFETY RISKS: Healthesystems data shows top physician-dispensed drug classes include opioid analgesics, NSAIDs, muscle relaxants, dermatologicals/topicals, and anti-ulcer medications. Many of these medications pose risk to the injured worker and are linked to poorer outcomes.
- REDUCE COSTS: Not only are direct costs of physician-dispensed medications significant, but they increase overall medical costs. A study of workers' comp claims in Illinois found that medical costs were 39% higher in claims with physician-dispensed medications.²
- OPTIMIZE DRUG REGIMEN: Medications processed through a retail pharmacy ensures a pharmacist can perform a drug utilization review for clinical appropriateness and potential drug-drug interactions.
- SUPPLEMENT STATE REFORMS: While state reforms are a part of the solution and have demonstrated some success, analyses show that physician-dispensing patterns tend to shift in reaction to these reforms, limiting the ability of reforms to control costs over the long-term.



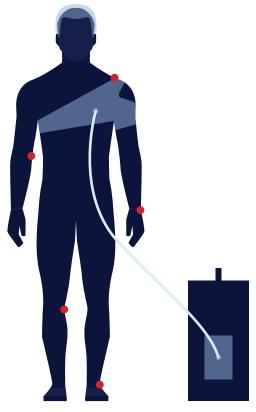
FAST FOCUS

Healthesystems continues to monitor top cost drivers among ancillary products and services, including durable medical equipment (DME). Trends demonstrate increased utilization of thermal compression devices within workers' comp, despite a lack of clinical evidence for their efficacy, resulting in unnecessary treatment and costs.

WHAT ARE THERMAL COMPRESSION DEVICES?

Thermal compression devices combine hot and cold therapies with pressure for the treatment of pain, inflammation, swelling, and circulation in the extremities (ankles, knees, elbows, shoulders, wrists). They are typically used following acute injury or a surgical procedure, making them attractive to healthcare professionals as a therapy option for the injured worker population. Physical therapy clinics may utilize these devices along with physical therapy or exercise regimens. However, these devices are also manufactured and marketed for at-home use.

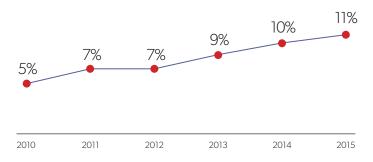
The devices consist of sleeves that wrap around a patient's extremities to provide pressure and cold and/or heat. Some devices come with a connector hose that attaches to a mechanized compression pump, but other devices simply circulate ice water. Regardless, the principles of pressure and temperature adjustment are still present.



GROWING COST DRIVER

Thermal compression devices have comprised a growing portion of overall DME spend over the last five years due to increased prescribing and utilization of these devices. Having insight into such trends can help guide strategies for controlling utilization and costs.

Percent of Overall DME Spend¹



In light of their growing use, what should claims professionals know about thermal compression devices?

WHAT ARE THE CONCERNS?

Thermal compression devices come at excessive costs without providing additional significant clinical benefit to most patients over traditional hot and/or cold therapies.

Unproven Clinical Efficacy

The American College of Occupational and Environmental Medicine (ACOEM) Practice Guidelines and the Official Disability Guidelines (ODG) consider the use of thermal compression devices to be purely investigational, with no significant clinical evidence proving that thermal compression devices provide greater therapeutic results than standard cryotherapy with ice packs or reusable gel cold packs.

Cost Considerations

Prices for thermal compression devices vary depending on model and purchasing channel, but devices can cost thousands of dollars. According to GameReady, their products retail for approximately \$1,000 for a two-week rental.² Upfront purchase or rental costs are not the only factor. Some thermal compression devices come with recurring costs of additional equipment, such as replacement pads, extra connector hoses, carrying cases, and more. These recurring costs can compound the overall costs associated with these devices over time, underscoring the continued need for visibility into the shifting cost drivers among ancillary services and products such as DME.



Thermal Compression Considerations

While different payers have different claims management strategies regarding thermal compression devices, it is helpful to be aware of this growing trend.

Know the products:

Claims professionals should familiarize themselves with thermal compression device models and manufacturers. Examples include:

- ▶ GameReady products
- VascuTherm (ThermoTek)
- Polar Care (Breg)
- Cryo/Cuff (D|O Global)
- VenaFlow (DJO Global)
- ▶ Bio Compression

Know the alternatives:

Consider the use of ice packs and reusable gel cold packs. According to evidence-based medical guidelines, thermal compression devices have no proven clinical benefit over these traditional hot and/or cold therapy treatments.

Know the exceptions:

In the event a prescriber determines a thermal compression device is medically necessary, payers can implement different strategies for managing utilization, such as limiting use to certain conditions and for short rental duration.

STATE OF THE STATES



The Industrial Commission recently posted guidance materials and flowcharts on the use of medical treatment guidelines and provider authorization processes. These resources can be found on their updated Medical Resource Office page at www.azica.gov.

Public Stakeholder Meeting

The Commission also held a public meeting for industry stakeholders for the purpose of gathering input on the introduction of legislation that would impact aspects of the Industrial Commission's operations. Many individuals provided input on recommended system changes, addressing medical treatment, reimbursement rules, utilization review, and dispute resolution.



The California Division of Workers' Compensation (DWC) released its initial draft of their drug formulary rule on August 26. The draft rule updated multiple sections of the Medical Treatment Utilization Schedule (MTUS), and included a Preferred Drug List. The Preferred Drug List and MTUS updates were modeled around guidelines published by the American College of Occupational and Environmental Medicine (ACOEM). Formulary highlights include:

- Preauthorization requirements and medical necessity for compound drugs and non-preferred drugs
- Prohibiting payers from requiring preauthorization for preferred drugs, while allowing payers to uniformly approve nonpreferred drugs within their utilization review (UR) plans
- New prescriber documentation requirements for brand drugs when a generic is available
- Preauthorization requirements for the physician-dispensing of most medications
- Rules for transitioning patients from non-preferred medications to preferred-medications when appropriate

Stakeholders provided extensive feedback to the DWC via their online forum, and the DWC is considering this feedback before adopting a final rule which is expected to become effective by July 1, 2017. Additional medications may be added to the preferred drug list and more specific timeframes may be delivered regarding the transition process. A formal hearing will occur prior to the final disposition of the rule.

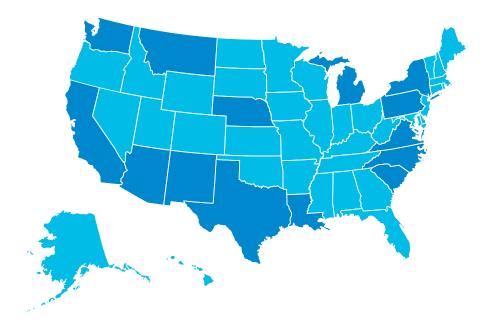


Governor Andrew Cuomo's administration has pushed a statewide effort to increase access to drug treatment resources. The effort began with the 2012 I-STOP bill, intended to decrease doctor shopping and diversion. The bill hoped to accomplish this goal by increasing prescriber utilization of the state's prescription drug monitoring program and by mandating the electronic prescribing of controlled substances. This summer, Cuomo signed a comprehensive package of bills expanding patient and first responder access to emergency drug treatment medications like naloxone, and requiring health insurers to use state-approved uniform criteria for coverage determinations when considering approval for substance abuse disorder treatment. Most relevant to workers' compensation patients is a new provision which prohibits physicians from prescribing more than a seven-day supply of opioids for acute pain treatment, while also requiring ongoing education in pain management for all prescribers. Similar legislation became law throughout various states in 2016, such as Connecticut, Rhode Island, Maine, Massachusetts, and New Hampshire.

In conjunction with these efforts, the New York State Workers' Compensation Board (WCB) updated its information packet to include state agency contact information for injured workers concerned about opioid dependency and substance abuse treatment services. The WCB also released a discussion document for public comment that proposes the implementation of a drug formulary, additional price controls on physician dispensers and compounds, and oversight of PBM programs.



At a recent quarterly carrier meeting, Texas Division of Workers' Compensation (DWC) regulators advised attendees about the status of a system-wide Compound Medications Audit. Matt Zurek, DWC Executive Deputy Commissioner, indicated that of the top ten prescribers of compounds, selected based on volume and billed amounts, seven have been escalated to a second review process by the Medical Quality Review Panel (MQRP) for suspected non-adherence to the Official Disability Guidelines (ODG). The other three cases are still under first review. DWC will publish the audit results once they become available. The Texas formulary requires all medications defined as investigational, experimental, or non-FDA-approved be subject to preauthorization. However, the Texas



formulary rules only require preauthorization for compounds with an "N" drug as an ingredient. This has created a loophole in that compounds by nature are not FDA-approved since they are custom made for the patient, yet they are often made with FDA-approved ingredients. The DWC has been approached by stakeholders about this issue since the formulary was initially adopted in 2011, but there is no indication at this time that the rule is subject to amendment in the near future. It remains to be seen if the findings from this audit will drive legislative or regulatory change in 2017.



The Washington Department of Labor and Industries (L&I) released trading partner agreement forms along with technical reporting requirements for medical bill payment data paid by self-insured entities or their third party administrators. L&I confirmed it will implement Medical Bill Electronic Data Interchange (EDI) using IAIABC Release 2.0 reporting standards. Testing for Medical Bill Reporting EDI will begin late 2016 with voluntary reporting beginning early 2017. Mandatory reporting will begin on July 1, 2017. Currently, there are no statutory requirements authorizing L&I to collect medical bill data, however, proposed rules will be drafted in the coming months and are expected to be adopted by July 1, 2017.

NCCI Updates Reporting Requirements

The National Council on Compensation Insurance (NCCI), along with several independent rating bureaus, announced two changes to their medical data call requirements. As of July, NCCI now offers a new indicator to determine if a payment was processed by a pharmacy benefit manager through a network pharmacy. NCCI also added new codes to capture payments made by carriers to injured workers for the reimbursement of medical marijuana. NCCI also announced that their Data Educational Program will be held from January 31 through February 3.

US DEPARTMENT OF LABOR Report Indicates State Programs Account for Cost Shifting

In early October, the US Department of Labor (DOL) released a report Does the Workers' Compensation System Fulfill its Obligations to Injured Workers? The DOL and the National Academy of Social Insurance hosted a public webcast to review the findings. According to the report "there is growing evidence that costs of workplace-related disability are being transferred to other benefit programs" like Medicare, Social Security Disability, and the medical coverages under the Affordable Care Act. The report is timely considering recent court decisions in Florida which have sparked a national debate about the adequacy of benefits. Legislation in a number of states now limits the duration of medical benefits, and other states have created statutory coverage exclusions on some injury types and exposures, leaving injured workers without recourse. The report delves into the details of those issues and how, despite the cost shifting, employer costs continue to rise nationally. The full report can be accessed at www.dol.gov.

2017 REGULATORY FORECAST

- $\blacktriangleright \quad \text{More bills will be raised on mandatory prescriber education}$
- Seven-day limits on acute pain opioid prescribing will continue to pop up
- Many states will consider drug formularies (LA, MI, MT, NY, NE, NC, SC, NM, PA, VA)
- Federal inquiries on manufacturer price gouging may drive changes in pharmaceutical regulation
- Treatment guidelines will continue to be discussed as states grapple with evidence-based medicine and consensus medicine
- Growing discussion will address issues related to compound drugs, physician dispensing and novel dose medications
- The national conversation of workers' compensation benefit adequacy will continue

BY THE NUMBERS

OPIOID OVERDOSE

Receiving NALOXONE

with long-term opioid prescriptions lowered emergency department visits by





Annals of Internal Medicine, 2016

DRUG SPEND

Specialty drug spending reached

\$121 billion in 2015



Centers for Disease Control and Prevention, 2016

New Hepatitis C drugs treated

250,000 people in 2015



IMS Health, 2016

LEGISLATION AND POLICY

Congress passed CARA, authorizing

\$181 MILLION

a year to fight the opioid epidemic



Comprehensive Addiction and Recovery Act (CARA), 2016

The CDC granted over

\$30 MILLION



TO 29 STATES

to improve prescription drug monitoring programs (PDMPs) and safety policies

Centers for Disease Control and Prevention, 2016

6 different compounding pharmacies paid fraud settlements from

\$2.1 - \$10 MILLION



Department of Justice, 2015-2016

REFERENCES

Cannabis Conundrums: Making Sense of Tangled Marijuana Legislation

- 1. Goodman E. Attorney: comp carrier pays for medical cannabis in a first for Minnesota. *WorkCompCentral*. May 3, 2016. https://www.workcompcentral.com/news/story/id/be104d33182cdbeb8717d1a1b-d473a8ad9882247
- 2. Goodman E. Workers' comp board approving reimbursement for medical pot. *WorkCompCentral*. May 9, 2016. https://www.workcompcentral.com/news/story/id/d5b0a73d9f-5230b928ab1403bd40d4642dce077b
- 3. Ceniceros R. Cannabis reimbursement trend grows. *Risk & Insurance*. June 24, 2016. http://www.riskandinsurance.com/cannabis-reimbursement-trend-grows/
- 4. *Maez v. Riley Industrial*. 2015-NMCA-049 347 P.3d 732- 54/29/21
- 5. State Medical Marijuana Laws. National Conference of State Legislatures web site. http://www.ncsl.org/research/health/state-medical-marijuana-laws.aspx. Published July 20, 2016. Accessed August 16, 2016
- 6. Rosenberg C, Burwell SM, Botticelli M. Joint Response Memorandum from DEA, U.S. Department of Health and Human Services, and Office of National Drug Control Policy to Marijuana Inquiries from Senator Elizabeth Warren. Published April 4, 2016. http://www.warren.senate.gov/files/documents/2016-4-4 response.pdf
- 7. DEA announces action related to marijuana and industrial hemp. Drug Enforcement Administration website. https://www.dea.gov/divisions/hq/2016/hq081116.shtml. Published Aug 11, 2016

How to Treat a Lady: Drug Therapy Risks for Women in Workers' Comp

- 1. Women's Bureau, U.S. Department of Labor. American women: Looking Back, Moving Ahead: The 50th Anniversary of the President's Commission On the Status of Women Report. March 2015. https://www.dol.gov/wb/PCSW-03-30-2015.pdf
- 2. Bureau of Labor Statistics. Nonfatal occupational injuries and illnesses requiring days away from work, 2013 [news release]. December 2014. http://www.bls.gov/news.release/archives/osh2_12162014.pdf
- 3. Centers for Disease Control and Prevention. Vital Signs: Prescription Painkiller Overdoses. July 2013. http://www.cdc.gov/vitalsigns/prescriptionpainkilleroverdoses/index.html
- 4. National Center for Health Statistics. Prescription Opioid Analgesic Use Among Adults: United States, 1999–2012 [NCHS Data Brief]. February 2015. https://www.cdc.gov/nchs/data/databriefs/db189.pdf
- 6. Bachhuber MA, et al. Increasing Benzodiazepine Prescriptions and Overdose Mortality in the United States, 1996-2013. American Journal of Public Health. April 2016. 106:686–688. doi:10.2105/AJPH.2016.303061
- 7. CDC. Vital Signs: Variation Among States in Prescribing of Opioid Pain Relievers and Benzodiazepines United States, 2012. July 2014. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6326a2.htm
- 8. Jones CM, McAninch JK. Emergency department visits and overdose deaths from combined use of opioids and benzo-diazepines. American Journal of Preventive Medicine. October 2015. 49(4):493-501. doi: 10.1016/j.amepre.2015.03.040. Epub 2015 Jul 3

- 9. Olfson M, King M, Schoenbaum M. Benzodiazepine use in the United States. JAMA Psychiatry. 2015;72(2):136-142. doi:10.1001/jamapsychiatry.2014.1763 December 17, 2014
- 10. Depression in women: understanding the gender gap. Mayo Clinic Web site. http://www.mayoclinic.org/diseases-conditions/depression/in-depth/depression/art-20047725. Published January 2016. Accessed May 6, 2016
- 11. Zhong W, Kremers HM, Yawn BP, et al. Time trends of antidepressant drug prescriptions in men versus women in a geographically defined US population. Archives of Women's Mental Health. 2014;17(6):485-492. doi:10.1007/s00737-014-0450-7
- 12. Pratt LA, Brody DJ, Gu Q. Antidepressant use in persons aged 12 and over: United States, 2005–2008. NCHS data brief, no 76. National Center for Health Statistics. October 2011
- 13. Centers for Disease Control and Prevention. Variation in Physician Office Visits By Patient Characteristics and State, 2012. September 2015. http://www.cdc.gov/nchs/products/databriefs/db212.htm
- 14. Gender Differences in Health Care, Status, and Use: Spotlight on Men's Health. The Henry J. Kaiser Family Foundation Web site. http://kff.org/womens-health-policy/ fact-sheet/gender-differences-in-healthcare-status-and-use-spotlight-on-menshealth/. Published May 31, 2013. Accessed May 20, 2016
- 15. Back SE, Payne RL, Wahlquist AH, et al. Comparative profiles of men and women with opioid dependence: results from a national multisite effectiveness trial. Am J Drug Abuse. 2011;37(5):313-23. doi: 10.3109/00952990.2011.596982
- 16. FDA Office of Women's Health. Dialogues on Diversifying Clinical Trials: Successful Strategies for Engaging Women and Minorities in Clinical Trials. September 2011. http://www.fda.gov/downloads/ScienceResearch/SpecialTopics/WomensHealthResearch/UCM334959.pdf

REFERENCES

- 17. Weinberger AH, McKee SA, Mazure CM. Inclusion of women and gender-specific analyses in randomized clinical trials of treatments for depression. J Women's Health. 2010. doi:10.1089/jwh.2009.1784
- 18. Artera J et al. Evaluation of how depression and anxiety mediate the relationship between pain catastrophizing and prescription opioid misuse in a chronic pain population. Pain Medicine. August 2015. doi: 10.1111/pme.12886

Thinking Outside The Claim: Using Multidimensional Data to Estimate Potential Opioid Misuse

- 1. Cooper S. Workers Compensation and Prescription Drugs: 2016 Update. NCCI Annual Issues Symposium; May 2016
- 2. Healthesystems. Estimating potential misuse of prescription opioids by injured workers in workers' compensation. Poster presented at the American Academy of Pain Medicine 2016 Annual Meeting; Palm Springs, CA
- 3. Chen JH, Humphreys K, Sha NH, Lembke A. Distribution of opioids by different types of medicare prescribers. *JAMA Intern Med.* 2016;176(2):259-61
- 4. White AG, Birnbaum HG, Schiller M, et al. Analytic models to identify patients at risk for prescription opioid abuse. *Am J Manag Care*. 2009;15(12):897-906

Focus On: Opioid Overdose and Dependence Therapies

- 1. Comprehensive Addiction and Recovery Act of 2016. S.524 114th Congress (2015-2016). https://www.congress.gov/bill/114th-congress/senate-bill/524. 2016
- 2. Legal interventions to reduce overdose mortality: naloxone access and overdose good samaritan laws. The Network for Public Health Law web site. https://www.networkforphl.org/_asset/qz5pvn/network-naloxone-10-4.pdf. June 2016

- 3. Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain United States, 2016. MMWR Recomm Rep 2016;65(No. RR-1):1–49. DOI: http://dx.doi.org/10.15585/mmwr.rr6501e1
- 4. Medication and counseling treatment naloxone. Substance Abuse and Mental Health Services Administration. http://www.samhsa.gov/medication-assisted-treatment/treatment/naloxone. Last updated March 3, 2016. Accessed September 8, 2016
- 5. Medication and counseling treatment buprenorphine. Substance Abuse and Mental Health Services Administration. http://www.samhsa.gov/medication-assisted-treatment/treatment/buprenorphine. Last updated May 31, 2016. Accessed September 8, 2016
- 6. Goodnough A, Zezima K. When children's scribbles hide a prison drug. *New York Times*. May 26, 2011. http://www.nytimes.com/2011/05/27/us/27smuggle.html. Accessed September 8, 2016
- 7. HHS announces new actions to combat opioid epidemic [press release]. Department of Health and Human Services. July 6, 2016. https://www.hhs.gov/about/news/2016/07/06/hhs-announces-new-actions-combat-opioid-epidemic.html
- 8. Gordon AJ, Sullivan MA. The off-label use of sublingual buprenorphine and buprenorphine/naloxone for pain. Providers' Clinical Support System for Medication Assisted Treatment. Last updated Nov 29, 2013. http://pcssmat.org/wp-content/uploads/2014/02/PCSS-MATGuidanceOff-label-bup-for-pain.Gordon.pdf

Myth Busters: Physician Dispensing Edition

- 1. Swedlow A, Gardner AB, Ireland J. CWCI Research Brief: Differences in outcomes for injured workers receiving physician-dispensed repackaged drugs in the California workers' compensation system. Oakland, CA: California Workers' Compensation Institute; February 2013
- 2. White JA, Tao X, Artuso RD, et al. Effect of physician-dispensed medication on workers' compensation claim outcomes in the state of Illinois. *J Occup Environ Med*. 2014;56(5)459-64
- 3. Prescribing errors are the most common medication errors in primary care practices: Research Activities, February 2009, No. 374. February 2009. Agency for Healthcare Research and Quality, Rockville, MD. http://archive.ahrq.gov/news/newsletters/research-activities/feb09/0209RA5.html
- 4. Munger MA, Ruble JH, Nelson SD, et al. National evaluation of prescriber drug dispensing. *Pharmacotherapy*. 2014; 34(10):1012-20
- 5. Wang D. Physician Dispensing in Workers' Compensation. WCRI. 2012: 12-24

Under Pressure: Scrutinizing the Rise of Thermal Compression Devices

- 1. Healthesystems findings, 2016
- 2. Cost Analysis of Cryotherapy and Compression Products. Game Ready. 2011. http://www.gameready.com/wp-content/uploads/2012/12/Cost_Analysis_Cryo_Compression_Prodcuts_White_Paper.pdf

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