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RxINFORMER

CURRENT AND EMERGING ISSUES IMPACTING WORKERS' COMP

SPRING 2014

Understanding Pain: NEUROREMODELING

Specialty Pharmacy
EMERGES IN
Workers' Comp

INTERACTIVE EXPERIENCE
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ALSO IN THIS ISSUE:

STEP Therapy &
Therapeutic Interchange
Improved Management of Appropriate Drug Therapy

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Uncover hidden opportunities to control complex issues such as Opioid Abuse | Opioid Misuse | Diversion of Drugs | Excessive Therapy

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NEW STRATEGIES NEEDED

MANY FACTORS DRIVE MEDICAL COSTS IN WORKERS' COMPENSATION

Medical costs continue to be the primary driver of total workers' compensation claim costs. Pharmacy and physical medicine costs are the largest and most amenable to thoughtful medical management and cost containment programs.

The outlook for pharmacy utilization and spending causes great concern considering various factors that exist — new branded versions of existing chronic pain medications continue to be developed and marketed; the opioid epidemic is still in the early stages of being addressed by a number of states and professional societies; and the growth of new specialty pharmaceuticals is starting to accelerate. Individually, these factors would be sufficient to continue driving pharmacy spending. When combined, they increase the urgency to develop greater awareness and innovative benefits management strategies to address each of them.

OPIOIDS CONTINUE TO POSE PROBLEMS

In this issue, we address the continuing challenge of over-prescribing of opioids. The new release of Zohydro™ is a big issue as it brings a long–acting version of hydrocodone to market and does so without the protection of tamper-resistance. We also focus on the primary issue of avoidance of the use of opioids as a routine measure to treat acute injury. The goal should be to minimize the number of injured workers who receive opioids initially; and for those who do, minimize the duration of treatment.

Once an injured worker passes through the acute phase and remains on opioids, the challenge is to minimize the dose and duration to avoid long-term use and all of the associated risks and costs. They can include prolonged disability, delayed recovery, escalating doses of medication as the effectiveness fades, opioid-related side effects, additional medications prescribed to address the side effects and lack of pain relief, and increased overall medical costs due to falls. They can also include other medical problems aggravated by chronic opioid use, accidental overdoses and hospitalizations.

ABOUT THE AUTHOR

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We cover these issues with excellent articles on the prevention and minimization of opioid prescribing as well as a guide for tapering and discontinuing opioids. Although there is no cookbook formula, there are guidelines for tapering and discontinuing opioid therapy that should be shared with prescribers. If prescribers are not comfortable following them, they should refer injured workers to specialists who have the expertise and experience to reduce and eliminate chronic opioid use.

There is also a very interesting article on neuroremodeling in response to pain and its treatment. Hopefully, the information will be extremely useful in better understanding what happens in the brain and how we can avoid or reverse this effect that occurs sooner than most of us realize. New strategies to address pain are critical to counter this effect.

SPECIALTY PHARMACY POSES A NEW CHALLENGE

One of the largest and most challenging new cost drivers that has been developing under the radar due to the focus on opioids is the growth of specialty pharmacy. The recent development of new biologics, other anti-viral medications, and immune suppressors and modulators will continue and escalate in the years ahead. Each new medication seems to start a new round of price increases for a course of therapy, let alone for long-term term treatment depending on the condition. We cover the developments related to the treatment of Hepatitis B and C, HIV/AIDS, cancer and arthritis. Although the overall percentage of pharmacy spending is relatively low thus far, the growth potential is huge and expected to become exponential. Payers will need to develop strategies to address this area of pharmaceutical treatment as quickly as possible.

REGULATORY UPDATES

You will also find updates on regulatory activity by the various states as well as interesting pieces on medical marijuana and its status in various states with our analysis and recommendations.

ANCILLARY BENEFITS MANAGEMENT CHALLENGES

Lastly, physical medicine and other ancillary services continue to be important cost drivers for payers. These are challenging areas to manage due to complexities around coding and transparency, let alone medical management. We start to address these in this issue and will continue to share our thoughts and recommendations in future issues and other publications.

Taken together, we believe this issue will provide insights and information to help all stakeholders in workers' compensation develop new strategies to address critical cost drivers now and in the years ahead.

MED WATCH

WORKERS' COMP PROFESSIONALS SHOULD KEEP AN EYE ON THESE MEDICATIONS

A number of drugs that could impact workers' compensation are under consideration by the FDA. The projected approval dates are estimates based on timelines established by the FDA for product reviews. New drug applications (NDA) for new chemical entities (NCE) are expected to be reviewed within 12 months of the NDA filing. The FDA has 10 months to review applications for new dosage forms of existing products. A status of priority review expedites the FDA process, shaving off four months from the 12-month review timeline for a NCE.[1] Several sources were used to provide the best estimate for timing of the new product and first-time generic approvals.[2,3,4]

MARCH 2014

Zohydro ER™ ✦
PAIN
hydrocodone bitartrate extended-release opioid
Note: Concern for potential abuse

Empagliflozin ✦
DIABETES
an oral medication for Type 2 diabetes
Note: This will be the third product in a new class of Type 2 diabetes medications.

APRIL

Afrezza® ✦
DIABETES
nasally inhaled ultra-rapid-acting insulin for Type 1 and 2 diabetes

Abiglutide ✦
DIABETES
once-weekly injectable for Type 2 diabetes

Pennsaid® 1% (diclofenac) ■
PAIN
a topical NSAID solution for osteoarthritis of the knee
Note: Manufacturer has already started marketing a 2% Pennsaid. It is anticipated that the 1% formulation will be discontinued.

Viracept® (nelfinavir)
SPECIALTY
oral antiviral for HIV/AIDS

MAY

CompleoTRT™ ✦
OPIOID SIDE EFFECTS
testosterone bioadhesive intranasal gel for testosterone replacement

Celebrex® (celecoxib) ■
PAIN
an NSAID
**May 2014 - December 2015*

Lunesta® (eszopiclone) ■
HYPNOTIC
hypnotic/sleep aid

JUNE

Bunavail (buprenorphine) ✦
PAIN
naloxone buccal film for treatment of opioid dependence
Note: May be used to treat pain as with similar products Suboxone® and generic versions.

Tedizolid ✦
ANTI-INFECTIVE
oral antibiotic (similar to Zyvox®) (priority review requested)

Ferric citrate coordination complex ✦
SPECIALTY
to reduce blood phosphate levels in patient with chronic kidney disease who receive dialysis

BEMA buprenorphine (buccal film) ✦
PAIN
opioid for severe chronic pain
Note: Concern for abuse potential.

JULY

Dihydroergotamine (Levadex®) inhaler ✦
PAIN
for acute migraine

Tavaborole ✦
ANTI-INFECTIVES
a topical antifungal product

LEGEND

■ FORECAST OF ANTICIPATED GENERICS
The following generic drugs may affect workers' compensation payers and are expected to be approved in 2014 and 2015. The complexities of patents and marketing exclusivity may alter these dates.

✦ PROJECTED APPROVAL OF NEW PRODUCTS
The new products noted in this timeline may be prescribed to treat workers' compensation patients. Payers should be aware of these medications.

SEPTEMBER

Naloxegol ✦
OPIOID SIDE EFFECTS
for opioid-induced constipation

CERC-301 ✦
PSYCHIATRY
for major depressive disorder (priority review granted)

Combivent® (albuterol/ipratropium) ■
COPD
a combination inhaler for COPD

Sufentanil sublingual microtablet system (Zalviso) ✦
PAIN
opioid for in-hospital pain management of moderate-to-severe acute pain

Note: The potential for availability outside of the hospital setting is unknown; If use outside of hospital is allowed, there is a risk for abuse, misuse & diversion.

OCTOBER

Symbicort® (budesonide/formoterol) ■
COPD
a combination inhaler product for COPD and asthma

Taigexyn® (nemonoxacin) ✦
ANTI-INFECTIVE
an antibiotic to treat community-acquired bacterial pneumonia and skin infections (priority review granted)

Abilify® (aripiprazole) ■
PSYCHIATRY
an atypical antipsychotic used to treat psychoses and an add-on to antidepressant therapy for major depressive disorder

NOTE: Date depends on market exclusivity and possible legal challenges to generic.
**October 2014 - April 2015*

NOVEMBER

Copaxone® (glatiramer) ■
SPECIALTY
for relapsing-forms of multiple sclerosis

Targiniq™ ER (oxycodone hydrochloride/ naloxone hydrochloride) ✦
PAIN
opioid controlled-release tablets for chronic pain

JANUARY 2015

Indomethacin submicron ✦
PAIN
formulation of an NSAID that has been available since 1965; for mild to moderate acute pain
Note: Anticipate high cost of this version of a 50-year old drug
**Late 2014-Mid-2015*

Namenda® (memantine) ■
HYPNOTIC/SLEEP AID
used to treat Alzheimer's disease
Note: In February 2014, Forest Laboratories announced discontinuation of the brand name 5 and 10mg tablets as August 15, 2014. The oral liquid and newer extended release capsule will remain on the market. Manufacturer's information available at www.namenda.com

MARCH

Renagel® (sevelamer) ■
SPECIALTY
to reduce phosphate blood levels in patients with chronic kidney disease who receive dialysis

Sustiva® (efavirenz) ■
SPECIALTY
for HIV/AIDS

AUGUST

Androgel® (testosterone) ■
OPIOID SIDE EFFECTS
testosterone replacement

DRUG ALERTS

NEW DRUGS APPROVED

The following new drugs received FDA approval:

Tivorbex™(indomethacin)
A nonsteroidal anti-inflammatory drug (NSAID) is indicated for the treatment of mild to moderate acute pain in adults.

Monovisc® (sodium hyaluronate)
A single-injection supplement to synovial fluid of the osteoarthritic joint. It is indicated for the treatment of pain resulting from osteoarthritis of the knee in patients who have failed to respond adequately to conservative, non-pharmacologic therapy and to simple analgesics such as acetaminophen. Similar to Orthovisc®, Synvisc®, Synvisc® One, Euflexxav, Hyalgan®, Supartz® and Gel-One®.

Xartemis™ XR (oxycodone/acetaminophen)
An opioid combination product in an immediate and extended release formulation that is approved for severe acute pain.

Qudexy™ XR (topiramate)
An antiepileptic drug indicated for the treatment of certain types of seizures.

SCHEDULE II PROPOSED FOR HYDROCODONE COMBINATION PRODUCTS

The Drug Enforcement Administration (DEA) proposes to reschedule hydrocodone combination products from Schedule III to Schedule II of the Controlled Substances Act, based on a recommendation from the Department of Health and Human Services and an evaluation of all other relevant data by the DEA. If finalized, this action would impose the regulatory controls and administrative, civil, and criminal sanctions applicable to schedule II controlled substances on persons who handle (manufacture, distribute, dispense, import, export, engage in research, conduct instructional activities, or possess) or propose to handle hydrocodone combination products.

PRODUCTS IN CLINICAL TRIALS

New drug applications will likely be filed in 2014 for a number of drugs currently in clinical trials. Based on approval guidelines, it is possible that these products could be approved in late 2014 or sometime in 2015.

AVP-825
PAIN
a drug-device combination product for acute migraine treatment

Clonidine gel
PAIN
for painful diabetic nephropathy
Note: Depending on cost and how effective it proves to be, this may be a new option for treatment of neuropathic pain and help curb opioid use.

Androxal (clomiphene citrate)
OPIOID SIDE EFFECTS
a non-testosterone treatment for secondary hypogonadism

ALO-02 (oxycodone hydrochloride/naltrexone hydrochloride*)
PAIN
extended release opioid capsule for moderate-to-severe low back pain
Note: Abuse-deterrent properties not as strong as Oxycontin. Submitted by Endo Pharmaceuticals

* There is concern for drug abuse with the oxycodone/naloxone and oxycodone/naltrexone. The clinical significance of abuse deterrence with naloxone or naltrexone has yet to be determined.[5,6]

SPECIALTY PHARMACY
EMERGES IN WORKERS' COMPENSATION

FAST FOCUS

The increased use of specialty medications is projected to continue as more specialty drugs enter the market. The drugs can be used to treat a number of conditions seen in workers' compensation. Payers will need to balance the patient benefits they offer with the high costs often associated with these products and proactively develop strategies to manage this growing trend.

It is common for new trends in the group health insurance market to migrate to workers' compensation. One such trend is the growth of specialty pharmacy in workers' compensation. Specialty medications are typically expensive and may require special handling, distribution, administration and patient management. They are often used to treat complex and rare conditions.

A GLOBAL PERSPECTIVE

Spending on specialty drugs has been growing at a high rate in recent years. Although prescribed for only one in every 100 commercial health plan enrollees, specialty medications account for an estimated 12 to 16 percent of commercial prescription drug spending in the U.S.[7] Total global spending on specialty drugs across all payers is expected to increase 30 percent in developed markets between 2012 and 2017.[8] Driving this trend are several factors that include increased utilization, price inflation and an abundance of new medications in the pipeline.

Spending growth on innovative specialty medicines will be one of the single biggest cost concerns for healthcare systems in developed markets. Similar increases in spending on specialty drugs are likely to filter into workers' compensation. Cost containment will be a priority as these medications can top several hundred thousand dollars annually for a single patient.[9]

Specialty drugs are used to treat injured workers for complex conditions ranging from cancer and multiple sclerosis to hepatitis, HIV and rheumatoid arthritis, among others. The potential benefits they offer should be considered in concert with their costs. In some cases, specialty drugs can provide significant benefits since they may offer the only effective treatment available. In other cases, less expensive but equally effective alternative therapies may offer a better choice.

THE ABUNDANT MEDICATION PIPELINE

The upward trend in specialty medications use will continue as more unique specialty drugs are launched. Pharmacy benefit managers (PBMs) and payers will need to closely monitor the medication pipeline so they can prepare properly for the introduction of these products. Consider the statistics – the FDA's approval of specialty pharmaceuticals outnumbered those for traditional medications in the last two years.

Currently, more than 5,000 total new medications are in the global drug pipeline;[10] specialty pharmaceuticals account for more than half of the medications currently in late-stage development; over a third are biological products.[11] There has been a commensurate decline in the number of new medicines entering the traditional sector.[12] With fewer traditional drugs and more specialty drugs receiving approval, it makes sense that workers' compensation will see an increase in specialty drug use.

COST INFLUENCERS AND MONITORING CHALLENGES

Specialty medications can be categorized as self-administered agents, office-administered agents, or agents administered by home health agencies directly in the patient's home. Self-administered agents are administered by the patient and typically include oral and self-injectable products. Office-administered agents generally apply to injectable and infusible medications.

Specialty drugs can be seen in pharmacy drug benefit data, and physician/hospital bill data — sometimes both. Administration of certain self-injectable biologic agents by rheumatologists in their office can increase payer costs because they are billed as part of a physician or hospital bill. This makes it more challenging for payers to manage utilization, as they may not have full visibility into a patient's detailed drug regimen.

Many oncologists also prefer to dispense oral chemotherapeutic agents in the office leading to costly billing under the medical benefit.[13] This type of dispensing — referred to as "buy and bill"/physician dispensing — leads to increased costs for the payer primarily due to the incentive for the physician to use it as a revenue source.[14] Physician dispensing of specialty drugs may occasionally be appropriate for certain office-administered agents; however, it is recommended that self-injectable specialty products be managed through the PBM. This approach will provide insight and transparency into utilization and cost, and help payers more effectively manage specialty products.

A GROWING CONCERN. A THOUGHTFUL APPROACH.

Specialty medications will continue to grow in importance and pose various challenges for all stakeholders. This rapidly emerging trend requires a thoughtful, patient-centric strategic approach. Employers, payers, physicians, claims professionals and PBMs can work together to effectively manage these drugs and achieve favorable outcomes. Enhancing and expanding existing drug benefit management tools are key building blocks for managing specialty drugs. This includes optimizing drug formulary design as well as incorporating step therapy strategies and medication adherence monitoring tools. Similar to managing any complex medical care for injured workers, improving quality of care and reducing overall costs is best achieved through a comprehensive and collaborative approach.

TOTAL GLOBAL SPENDING ON SPECIALTY DRUGS EXPECTED TO INCREASE

30% **IN DEVELOPED MARKETS**

2012 - 2017

SPECIALTY PHARMACY STREAMS INTO WORKERS' COMP

Frequently, trends seen in the group health insurance market eventually trickle their way into the workers' compensation industry. A timely example of this can be seen in the growth of specialty medication. In group health, specialty medication use is expected to increase, with an anticipated 30 percent increase in spending over the next five years. Drivers of this trend will continue to be multifactorial: increased utilization, price inflation and the implosion of the pipeline for new medications. Follow the infographic below to learn more about this trend:

GROUP HEALTH

The use of specialty medications to treat complex conditions is prevalent in group health

More than 5,000 new medications encompassing 8,000 projects are in the pipeline globally

The breakdown of the medication pipeline includes, but is not limited to, the following therapeutic categories:

These medications provide novel or alternative treatment options

WORKERS' COMPENSATION

Specialty medications are funneling their way into workers' comp. For most payers, less than 0.5% of prescriptions filled in 2013 were for specialty medications, yet they accounted for over 2% of total prescription drug expenditures

In workers' comp specialty medications may be prescribed to treat these conditions:

- HEPATITIS C
- HIV/AIDS
- INFLAMMATORY CONDITIONS
- BLOOD CLOTS
- CANCER
- RESPIRATORY CONDITIONS

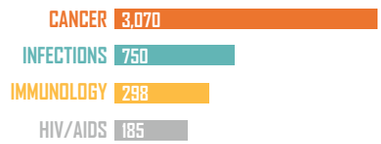
Over the past several years, the cost and use of specialty medications has steadily increased

BY THE NUMBERS

MORE THAN **5,000** NEW **MEDICATIONS** IN THE GLOBAL PIPELINE

BY 2016 **SPECIALTY PHARMACY** MAY ACCOUNT FOR MORE THAN **30%** OF GROUP HEALTH MEDICATION SPEND

THE MEDICATION **PIPELINE** INCLUDES NEW MEDS IN THESE **THERAPEUTIC CATEGORIES:**



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Healthesystems clinical findings. February 2014.

IMPLICATIONS FOR WORKERS' COMP

Specialty medications can address many unmet needs for patients that are either non-responsive to existing treatment therapies, or for those patients with conditions for which there were no treatment options in the past. The potential benefits can be great, but so can the cost

Payers and PBMs must proactively address the rising costs and utilization of this rapidly evolving trend and adopt integrated, patient-centric solutions that can improve outcomes

SPECIALTY DRUGS MAY BE BENEFICIAL FOR THE **PATIENT**

BENEFITS INCLUDE:

ADDRESS UNMET PATIENT NEEDS
SHORTER DURATION OF TREATMENT
MAY CURE/IMPROVE CONDITIONS

NEW HEPATITIS C DRUG WILL COST MORE THAN **$25,000** FOR A MONTH'S SUPPLY

SPECIALTY DRUGS CAN TOP **SEVERAL HUNDRED THOUSAND** DOLLARS ANNUALLY FOR A SINGLE PATIENT

TOP 10 SPECIALTY MEDICATIONS TYPICALLY SEEN IN WORKERS' COMPENSATION

by % of Specialty Spend

Generic Names

ANTICOAGULANT USED TO TREAT DVT BLOOD CLOTS POST SURGERY	ENOXAPARIN SODIUM	32%
MAINTENANCE THERAPY IN ADULTS WITH EMPHYSEMA	ALPHA1-PROTEINASE INHIBITOR	15%
USED TO TREAT MODERATE TO SEVERE ALLERGIC ASTHMA	OMALIZUMAB	11%
PREVENT ORGAN REJECTION OR TOPICAL FOR 2ND LINE TREATMENT OF ECZEMA	TACROLIMUS	9%
TREATMENT OF PAIN IN OSTEOARTHRITIS OF THE KNEE AS 2ND LINE THERAPY	HYLAN	8%
TREATS MODERATE TO SEVERE RHEUMATOID ARTHRITIS, CHRON'S DISEASE	ADALIMUMAB	8%
TREATS PATIENTS WITH AIDS FOR THE TREATMENT OF CMV RETINITIS	VALGANCICLOVIR HCI	7%
PREVENTS ORGAN REJECTION	MYCOPHENOLATE MOFETIL	7%
TREATS DEEP VEIN THROMBOSIS	FONDAPARINUX SODIUM	5%
HEPATITIS C	TELAPREVIR	<1%

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MEDICAL APPLICATIONS OF SPECIALTY DRUGS
IN WORKERS' COMPENSATION

FAST FOCUS

Certain complex conditions commonly seen in workers' compensation claims may derive benefit from treatment with specialty drugs.

Specialty drugs can be used to treat complex medical conditions that are seen in workers' compensation claims populations. Some conditions are directly related to workplace injuries or illnesses, such as HIV, hepatitis B and C and cancer. Others may be indirectly related, such as pre-existing rheumatoid arthritis or multiple sclerosis that may be aggravated by a workplace injury or illness.

WHO IS AT RISK FOR WORK-RELATED CANCER?

Workers in these fields have a proportionally higher risk of cancer deaths compared to workers in other industries.

- Chemical manufacturing
- Dye manufacturing
- Electronic computing
- Engineering
- Furniture manufacturing
- Healthcare
- Leather industry
- Machinery equipment
- Machinery manufacturing
- Printing
- Public safety
- Shipbuilding
- Social assistance
- Steel manufacturing
- Textile manufacturing
- Transportation equipment

*Sources: National Occupational Mortality Surveillance System & Sheffield Occupational Health Advisory Service

CANCER

Certain occupations may place workers at increased risk for developing cancer. According to the CDC, four percent of the cancer deaths in the United States are thought to result from work-related exposure.[15] The CDC indicated that the numbers may actually be higher because they do not capture all occupations and the majority of the research was conducted in the manufacturing industry.

The increase in work-related cancers and the development of more successful cancer therapies are expected to have a large impact on the workers' compensation population. According to estimates, the cost of an eight-week chemotherapy treatment may be as high as $30,000, depending on the type of cancer and the chemotherapeutic agent.[16] For specific cancers such as multiple myeloma, some of the newer agents are estimated to cost over $100,000 per patient per year.[17] The National Cancer Institute estimates that direct medical cancer-related costs in 2009 totaled $86.6 billion annually.[18]

The FDA approved several cancer agents in 2013 including obinutuzumab (Gazyva™) for chronic lymphocytic leukemia and ibrutinib (Imbruvica™) for mantle cell lymphoma. Many other specialty medications are currently in development for treatment of these and other cancers such as lung cancer, renal cell carcinoma, melanoma, head and neck cancer, and kidney cancer.[19]

HIV AND HEPATITIS

Some workers are exposed to blood borne pathogens via needle sticks or other types of direct contact that may cause conditions such as hepatitis B and C and HIV. These patients may need post-exposure prophylaxis (PEP) treatments to reduce their risk of developing HIV or hepatitis.

Depending on the condition, PEP can be provided via vaccines or immune globulins.[20] For HIV, a four-week regimen of three antiviral drugs is required and associated costs can reach $1,000.[21] Unfortunately, PEP is not always effective and exposed workers' may develop the actual conditions which can lead to lifelong treatment and greatly increased costs.[22] The lifetime treatment costs for an HIV-infected person are estimated to be between $253,000 and $402,000.[23] Patients who develop HIV are also at increased risk for co-infection with hepatitis C.[24] Sofosbuvir (Sovaldi™) and simeprevir (Olysio™) were recently approved to treat patients who develop hepatitis C.[25] The cost of these agents can be very high. For example, Sovaldi treatment can cost between $84,000 and $168,000 for the full regimen, depending on the strain of the virus.[26]

MULTIPLE SCLEROSIS

Multiple sclerosis (MS) and other inflammatory conditions can be caused or worsened by certain types of occupational exposure. One study indicated that workers in the agricultural segment — especially dairy-workers — may have higher risks for developing MS.[27] Another study suggested that agricultural workers have higher risks for MS due to pesticide exposure.[28] This study also found that workers such as shoe and leather workers and mechanics who are exposed to certain organic solvents may be at higher risk for developing MS. Work-related stress also has the potential to exacerbate MS. Stress in general has been linked to worsening symptoms of inflammation in MS patients.[29]

Treatment of MS is estimated to range from $8,528 to $54,244 per patient per year, of which 77 percent are direct costs

and include prescription medications.[30] Total lifetime treatment costs for a patient with MS are estimated to be $2.2 million.[31] The reasons behind the growing costs include the increased availability of new drugs such as dimethyl fumarate (Tecfidera®) and teriflunomide (Aubagio®), as well as the improved survival of patients afflicted with the disease. In addition to treatment of the disease itself, many MS patients will also require symptomatic treatment of bladder dysfunction, fatigue, emotional changes, spasticity and pain, which may contribute to the high lifetime treatment costs.[32]

OSTEOARTHRITIS AND RHEUMATOID ARTHRITIS

Development of osteoarthritis (OA) is associated with certain occupational tasks and is often considered a compensable work-related injury.[33] It is more common in construction, agriculture and some sectors of the service industry.[34]

Rheumatoid arthritis (RA), while not directly caused by a work-related injury, may lead to disability and lost time at work.[35] It is estimated that two thirds of workers with RA have experienced some level of work loss over a one-year period as a result of the inflammatory disorder.[36] Physical activity is thought to benefit arthritis patients.[37] Therefore, patients who experience a work-related injury that causes them become sedentary may experience exacerbation of an arthritic condition and make treatment for it compensable. The economic burden related to lost productivity in RA patients is high, with some companies experiencing losses of $1.69 million dollars over the course of one year.[38]

ESTIMATED COST PER PATIENT PER YEAR WHEN SPECIALTY MEDICATIONS ARE INDICATED MAY BE

MULTIPLE MYELOMA
$100,000
MULTIPLE SCLEROSIS
$8,528 - $54,244
OSTEOARTHRITIS & RHEUMATOID ARTHRITIS
$24,000

Treatment of both types of arthritis frequently relies on specialty medications. Synvisc®, Orthovisc® and Euflexxa® are sometimes utilized for more severe cases of OA. Costs for these injections typically exceed $1,000 per single joint treatment and may be needed over the course of several weeks. Nationwide spending estimates range from $3.4 to $13.2 billion annually for all job-related OA costs because of its high incidence.[39]

Biological agents including adalimumab (Humira®), etanercept (Enbrel®) and infliximab (Remicade®) are used to treat RA. Several of these agents have been shown to improve patients' abilities to perform their jobs.[40] Early intervention in rheumatoid arthritis is essential, as a disproportionate amount of work-related disability occurs early in the disease process.[41,42] While the costs associated with these treatments can be over $2,000 per patient per month, it is hoped that newer RA therapies will help patients achieve earlier remission of the disease and reduce lost work time.[43]

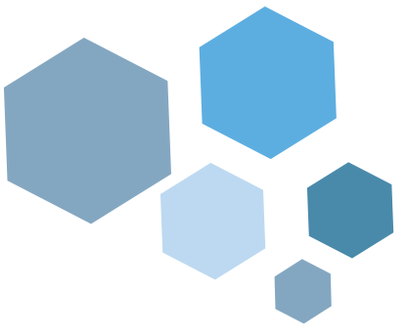
PERSONALIZED MEDICINE

Perhaps the most novel group of specialty drugs are those developed to treat a subgroup of patients based on unique patient or disease characteristics. Only a handful of these personalized medications have been approved in the past decade; however, this untapped area is beginning to gain traction and deserves close attention.

Personalized medicine often involves genetic testing which may provide insight into selecting the most appropriate drug for the patient, any potential dose changes that may be required, as well as avoiding certain adverse events. Two specialty drugs developed to treat lung cancer, erlotinib (Tarceva®) and crizotinib (Xalkori®), represent examples of a personalized approach to drug therapy by targeting specific mutated cancer genes.[44] Similarly, certain HIV drugs like maraviroc (Selzentry®) are only effective in patients with certain mutations of the HIV virus. Other HIV drugs like abacavir (Ziagen®) may require patients to undergo genetic testing to rule out mutations that may put them at risk for severe allergic reactions that may result from that particular drug.

CONCLUSION

As more specialty drugs are released to the market, the number of conditions they will be indicated to treat is likely to grow. Healthesystems will continue to monitor this growing trend and provide the appropriate decision support tools for the proactive management of workers' compensation-related conditions.



THERAPY AND THERAPEUTIC INTERCHANGE

IMPROVED MANAGEMENT OF APPROPRIATE DRUG THERAPY

FAST FOCUS

Step therapy and therapeutic interchange programs provide valuable opportunities for payers to provide injured workers with appropriate therapies and limit use of expensive prescription drugs to patients who need them. .

A number of prescription and over-the-counter drug therapies on the market offer similar therapeutic benefits at costs that vary widely. Careful analysis of the characteristics, benefits and costs of each drug and a review of evidence-based treatment guidelines can provide a strong foundation for implementing step therapy and therapeutic interchange programs. These innovative programs help payers and prescribers partner to provide patients with more appropriate drug therapy in a cost-conscious manner.

STEP THERAPY CASE SCENARIO

Sam is a 28-year old office worker. He was prescribed Celebrex for a work-related back strain. His employer's PBM implemented a step therapy program that flagged the Celebrex prescription for prior authorization when it was entered by the retail pharmacy. The PBM reviewed the claim eligibility data to determine if Celebrex was an appropriate choice. The review revealed that Sam was young and had no previous history of traditional NSAID use or GI issues. That led to a determination that Celebrex was not an appropriate initial therapy for him. The pharmacy was asked to contact the prescriber for a less costly traditional NSAID.

In the example, Sam needed an NSAID, but did not need the protective properties offered by Celebrex. Of the population using NSAIDs, the subset that requires those properties is very small. It includes older patients, patients with a history of GI complications and patients who have not benefited from or tolerated traditional NSAID therapy. Celebrex therapy should be reserved for those patients.

Healthesystems conducted a pilot step therapy program for Celebrex that garnered an average savings of 81 percent. In nearly 70 percent of cases, Celebrex prescriptions were not filled or were filled with a generic NSAID substitute after intervention.

STEP THERAPY

Step therapy relies on established evidence-based treatment guidelines to define the order in which drugs should be prescribed for certain conditions. The program typically guides physicians to prescribe lower cost, lower risk drugs as a first step. They can incrementally move to prescribing higher cost, higher risk drugs on subsequent steps until the patient responds favorably.

Celebrex® is a good example of a drug that can be well controlled through step therapy. It is the most expensive of the nonsteroidal anti-inflammatory drugs (NSAID) available to treat acute musculoskeletal injuries such as knee, back and shoulder sprains and strains, which represent the majority of first-time workers' compensation claims.

Celebrex is perennially in the top five NSAIDs prescribed.[45] It has a unique characteristic that protects against stomach ulcers — a chief side effect of long-term NSAID use. No other NSAIDs offer this protection. Since its release in 1998, Celebrex has been widely used to help avoid the adverse gastrointestinal (GI) effects of traditional anti-inflammatory medications. The traditional or non-selective prescription and over-the-counter alternative NSAIDs available include ibuprofen (Motrin®), meloxicam (Mobic®) and naproxen (Aleve®).

THERAPEUTIC INTERCHANGE

As more drugs become available within individual therapeutic drug classifications, there is often a large cost disparity among medications. When all characteristics are equal, cost can become the determining factor in therapy selection.

Therapeutic interchange incorporates this logic and presents another opportunity for payers to reduce pharmacy costs. Therapeutic interchange involves substituting requests for higher cost agents with lower cost alternatives. The program establishes a protocol for prescribing the least costly member of an individual drug classification — as long as the drug contains pharmaceutically-similar agents and has a similar or identical mechanism of action. These similarities often produce identical clinical benefits.

PROTON PUMP INHIBITORS

The cost of therapy with proton pump inhibitors (PPI) can be better controlled through therapeutic interchange. PPIs reduce stomach acid production. They benefit patients with gastroesophageal reflux disease (GERD) or who are taking NSAIDs because they protect against NSAID-induced stomach upset. Six prescription formulations are available. Prilosec® and Prevacid® also have over-the-counter formulations.

Prescription Nexium® was the number two drug prescribed in the US in 2013.[46] Gastroenterology experts agree that all PPIs confer a similar clinical benefit. Given the widespread use of prescription PPIs, requesting substitution for an OTC formulation through therapeutic interchange can result in substantial annual savings.

COST COMPARISON OF PROTON PUMP INHIBITOR THERAPY

A review of the 30-day cost of therapy with proton pump inhibitors illustrates the potential impact of therapeutic interchange.*

Agent	RX (AWP Cost for 30-day supply)			OTC (AWP Cost for 30-day supply)	
Omeprazole	Prilosec®	20mg	**$245.32**	Prilosec OTC®	**$28.96**
	Omeprazole	20mg	**$124.10**		
Lansoprazole	Prevacid®	15mg	**$301.54**	Prevacid® 24HR	**$28.96**
	Prevacid® Solutab	15mg	**$301.65**	N/A	
Dexlansoprazole	DexilantTM	30mg	**$200.78**	N/A	
Esomeprazole	Nexium®	20mg	**$284.09**	N/A	
Pantoprazole	Protonix®	40mg	**$253.34**	N/A	
Rabeprazole	Aciphex®	20mg	**$419.88**	N/A	

* Note: AWP costs can change over time. AWP cost reflects rates at the time of publication

Step therapy and therapeutic interchange have been widely used in group health to support clinical practice guidelines. They hold real potential for workers' compensation payers to ensure quality care and limit use of costly prescription drugs to patients who need them.

MEDICAL MARIJUANA:
A PRIMER FOR WORKERS' COMPENSATION

FAST FOCUS

As more states move to legalize marijuana for medical or recreational use, the potential clinical risks for patients and financial implications for workers' compensation payers will need to be considered carefully.

IS MARIJUANA SAFE FOR USE IN WORKERS' COMPENSATION?

Marijuana (Cannabis sativa) contains over 400 chemical components. Marijuana contains a mix of diverse chemical compounds called cannabinoids that also includes delta-9-tetrahydrocannabinol (THC), the most psychoactive component of marijuana and the one thought to cause the feeling of being "high" that users experience.

Marijuana is classified as a Schedule I substance under the Controlled Substances Act. Other Schedule I substances include heroin, methylenedioxymethamphetamine (commonly called ecstasy) and lysergic acid diethylamide (commonly called LSD). These drugs have a high potential for abuse, lack accepted medical uses, and are not accepted as safe for use under medical supervision.[47]

STUDY RESULTS ARE INCONCLUSIVE

Studies that examined the benefits and harm posed by marijuana use produced conflicting results. Some found in favor of marijuana use for medicinal purposes but were small-scale, conducted on animals, or lacked the statistical power needed to make a solid conclusion. Other studies showed a possible synergistic effect between the cannabinoid and opioid systems.[48,49,50] These studies suggested the potential for lower opioid doses, fewer side effects, and delayed tolerance, but were not large-scale in nature or were not conducted on humans so their conclusions cannot be relied upon regarding benefits to humans.

No large-scale randomized controlled human trials have been conducted that sufficiently ease concerns about the inherent risks of marijuana use. This is a factor in failed efforts to legalize marijuana for medical use on a federal level. The FDA requires all drugs seeking approval to undergo rigorous controlled trials to prove both safety and efficacy. Approval of marijuana at the state level bypassed this important safety process.

The answers to the questions at the top of page 21 and other questions included in the FDA approval process are important. Without them, physicians are left to employ a trial and error approach.

We do know that the effects of smoked and ingested marijuana are not equal. The chemical processes that occur in the body change with the route of administration. We also know that the techniques used to smoke marijuana can lead to dosage

UNANSWERED QUESTIONS

Marijuana also lacks the standardization required in the FDA-approval process. Important questions are left unanswered such as:

- How should marijuana be dosed?
- Is there a dose-response effect?
- How much marijuana is toxic or will cause a harmful effect?
- What is the chemical purity or acceptable batch variations?
- What are the best and worst routes of administration?
- What are the side effects?
- What are potential contraindications for use and/or potential drug-interactions?

VARIED RISKS

The potential for increased utilization of marijuana should raise concerns about possible adverse risks with payers. Marijuana use can cause the following:

- delay an injured worker's return to work[54]
- elevate risks for lung cancer when smoked[55]
- induce psychosis and other mental health disorders[56]
- lead to addiction or diversion[57,58,59]
- contribute to motor vehicle accidents[60]

inconsistencies. The depth of inhalation and time before exhalation can cause significant variations in the amount of the drug received. The side effects, duration of action, associated "high" and potential drug interactions also vary. More study is needed.

EXPECTATIONS FOR WORKERS' COMPENSATION

The FDA has not approved any uses for marijuana. Neither the American College of Occupational and Environmental Medicine (ACOEM)[51] nor Official Disability Guidelines (ODG) recommends its use. Furthermore, it is illegal under federal law for a physician to prescribe marijuana or for anyone to sell or use it. A growing number of states have legalized the sale and use of marijuana within the state. Technically, federal law supersedes state law; however, the federal government has informally indicated it will not interfere in those states.

Approved indications for medical use vary by states in which it is legal. Some have open-ended indications that allow determination on a case-by-case basis. Others use vague language to describe approved uses and leave considerable room for interpretation. For example, California law states that medical marijuana is approved for "chronic or persistent medical conditions that substantially limit a person's ability to conduct one or more major life activities as defined in the Americans with Disabilities Act of 1990, or if not alleviated, may cause serious harm to the person's safety, physical or mental health."[52] This could be interpreted to include severe, chronic or debilitating pain; muscle spasms/spasticity; seizures; post traumatic stress disorder (PTSD); migraines; arthritis; and other conditions commonly seen in workers' compensation populations. In Colorado, 94 percent of the 108,000 registered medical users in 2012 qualified based on a diagnosis of severe pain.[53]

It is not likely that medical marijuana will replace mainstay therapies in the near future. There is however, the potential for it to be recommended as an alternative therapy in cases where other approved therapies failed, or as adjunctive therapy.

Concerns have also been expressed about adverse drug-disease interactions and the dangerous cumulative adverse effects that can occur when marijuana is used concomitantly with therapies commonly prescribed in workers' compensation — opioid analgesics, sedative-hypnotics and muscle relaxants.[61] Interactions with other drugs can alter the effects of marijuana as well as the duration and intensity of the effects.

RECOMMENDATIONS FOR PAYERS

Healthesystems recommends against approving claims for medical marijuana in light of the absence of FDA-approved uses. Future legislative changes could require approval in some states under some circumstances. Payers would be prudent to work with their pharmacy benefit manager (PBM) to proactively develop a marijuana strategy and establish policies and procedures for handling any future marijuana claims. Documentation of medical necessity, step therapy, signed agreements, urine drug screening and the like could be incorporated. Educational materials and guidance for claims professionals on how best to handle such claims should be part of the effort.

A REGULATORY OVERVIEW OF MARIJUANA

FAST FOCUS

States have taken varied approaches to regulating use or possession of marijuana. At the federal level, marijuana remains an illegal substance under the Controlled Substances Act. This conflict between state and federal regulations could pose challenges for workers' compensation in the future.

California became the first state to legalize the medical use of marijuana when voters passed Proposition 215 in 1996. Advocates claimed victory on behalf of terminally ill patients and others enduring chronic pain even as critics argued that the campaign represented little more than a ruse to legalize recreational use.

LEGALIZATION IS GAINING GROUND

Policy disagreements have continued and proponents of medical marijuana have carried the day. Those in favor of legalization claim that medical marijuana can be used to alleviate symptoms of everything from chronic pain to AIDS to Alzheimer's disease. American voters and their elected officials watched commercials featuring suffering patients and largely decided in favor of legalization.

As of the beginning of 2014, 20 states and the District of Colombia legalized the use of marijuana for medical purposes. Bills were filed in 17 additional states to legalize marijuana for medical purposes. Colorado and Washington authorized recreational use under specified guidelines. Maryland and Alabama took the unusual step of passing legislation that allows the medical need for marijuana to be used as a legal defense for possession charges, though marijuana use and possession is not legal in those states. Four other states have similar legislation pending. See map on page 24.

STATE VS. FEDERAL LAW

Despite legalization efforts by various states, the status of medical marijuana has remained somewhat cloudy due to conflicting federal and state law. Marijuana remains an illegal substance under the Controlled Substances Act. Because it is a Schedule I controlled substance, physicians cannot write a prescription for it. Physicians "recommend" or "refer" a patient for treatment rather than prescribe marijuana in states where medical use is legal.

In 2013, the Department of Justice issued an update to its marijuana enforcement policy indicating that it would defer to the regulatory schemes of states that have adopted legalization programs. Federal regulators have also taken steps to clear the way for businesses engaged in state-authorized marijuana business activities to use the banking system without fear of federal recrimination.

PROMINENT OPPONENTS

While support for medical marijuana is gaining steam, two reputable organizations are standing strong against legalizing marijuana. The American Medical Association (AMA) recently reaffirmed its opposition stating that "cannabis is a dangerous drug, and as such, is a public health concern."[62] A position paper released by the American Psychiatric Association (APA) stated "medical treatment should be evidence-based and determined by professional standards of care; it should not be authorized by ballot initiatives."[63] The APA paper also included a thought-provoking statement about the lack of any FDA-approved drugs that are smoked. The Drug Enforcement Administration (DEA) also upholds its position that "smoked marijuana is not medicine."[64]

APPROVED SOURCES

Approved sources for marijuana vary by state. It can be obtained in dispensaries, through personal cultivation or directly from a caregiver — though some state laws remain silent on where marijuana can be purchased. Currently, billing is not processed

MORE INFO

Healthesystems provided in depth information about the clinical aspects of medical marijuana in an article that appeared in the Spring 2012 *RxInformer* clinical journal. Access it at www.healthesystems.com/rxinformer

through traditional retail pharmacies and Healthesystems has not processed any claims for medical marijuana.

Some states permit a licensed pharmacist to own or run a marijuana dispensary. Connecticut law mandates that a dispensary be run by a state-licensed pharmacist.[65] New bills have been proposed in some states to allow marijuana to be dispensed in a pharmacy. The Michigan Senate passed a bill that would allow pharmacies to dispense marijuana; however, an integral part of the legislation will likely block implementation. It requires a reclassification of marijuana to a Schedule II substance by the Drug Enforcement Administration — a move that is not expected anytime in the near future, if ever.

Close monitoring is needed to determine if injured workers are using marijuana, regardless of the source. Such use is likely escaping the safety checks provided by pharmacists and PBMs.

TRACKING USERS

In most states where medical marijuana use is legal, users are required to register. California and Maine make registration voluntary and Washington has no registration requirement. Some states accept other states' registration ID cards. If and how many claimants currently receive self-paid medical marijuana is largely unknown. This raises the concern for potential drug-drug interactions, drug-disease interactions, and possible abuse that are unidentifiable to payers.

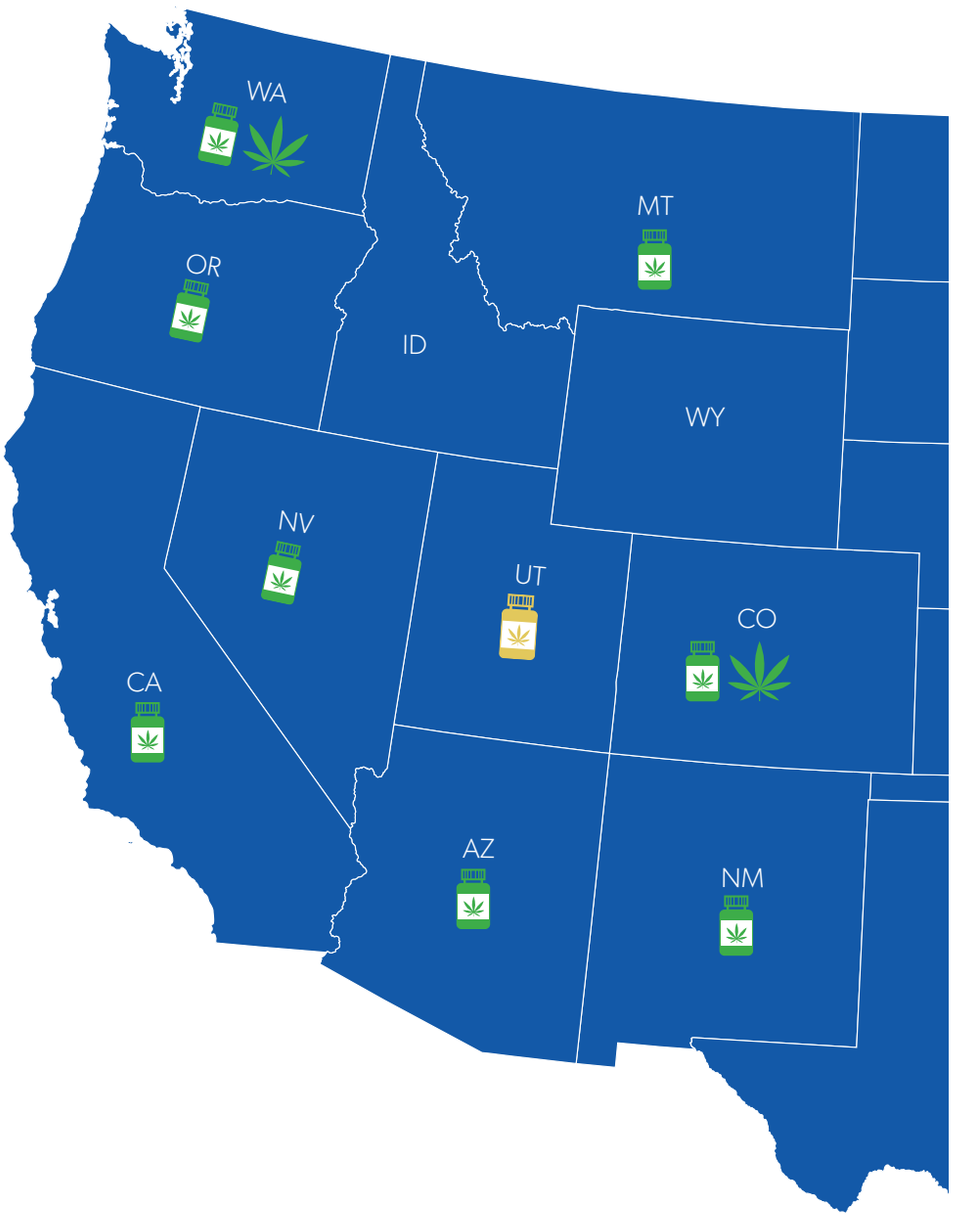
LEGAL IMPLICATIONS FOR PAYERS

While the continued illegality of marijuana at the federal level has provided payers with ample reason to decline to cover medical usage, it will be interesting to see if the evolving federal position will make such blanket denials more problematic in the long term. In the short term, the lack of FDA approval, combined with the fact that marijuana lacks the clinical trials required of all FDA-approved drugs, provides considerable protection for payers who do not wish to cover it.

Most payers appear to be complying with federal law and are not providing insurance coverage for medical marijuana. Several legal disputes have challenged this position and raised the question as to whether claimants should receive coverage for medical marijuana under their workers' compensation claim.

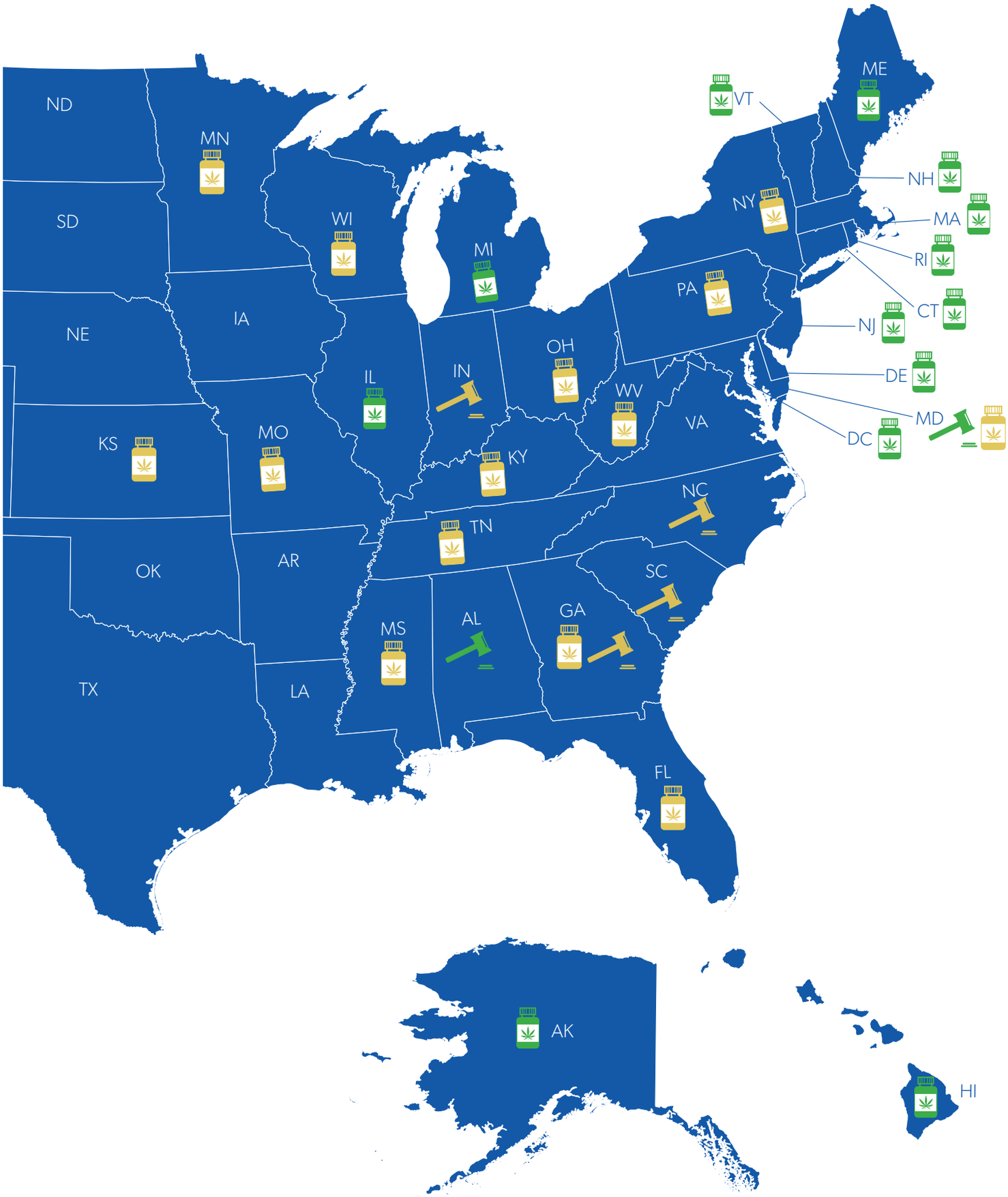
The IAIABC Survey of Medial Marijuana and Workers' Compensation lists states with specific rules regarding the payment of medical marijuana for injured workers. According to the April 2013 survey, Michigan, Montana, and Vermont have rules in place that allow or mandate denial of coverage for medical marijuana under workers' compensation.[66] The survey also lists examples of disputes regarding compensation for medical marijuana or related expenses such as registration fees or out-of-pockets costs related to a person growing his or her own marijuana plants. Court decisions have been inconsistent and rulings have been found in favor of both claimants and payers. Healthesystems will continue to monitor and report on legal changes and challenges.

LEGAL STATUS OF MARIJUANA & PENDING LEGISLATION



KEY

- Marijuana is legal for medical use
- Marijuana is legal for recreational use
- Marijuana is not legal in these states but possession of marijuana for medical purposes can be used as a legal defense
- Legislation is under consideration to legalize marijuana for medical use
- Legislation is under consideration to allow possession of marijuana for medical purposes to be used as a defense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AT A CROSSROADS IN PAIN MANAGEMENT

AN OPIOID TAPERING CASE SCENARIO

FAST FOCUS

A physician followed an opioid tapering plan to reduce an injured worker's morphine equivalent dose (MED) by 50 percent. He is at a crossroads in his efforts to reduce MED further because alternative therapies are needed.

Case Scenario Background: Dr. Jones inherited Patient X six months ago when the patient moved to a new community. The patient had suffered a shoulder and neck strain at work two years ago and continues to experience radiating pain. Her drug regimen includes multiple opioids and a muscle relaxant. The patient became clinically depressed and psychiatric drugs were added to her drug therapy; however, she did not take them regularly and her depression worsened.

CLINICAL GUIDANCE FROM THE PBM

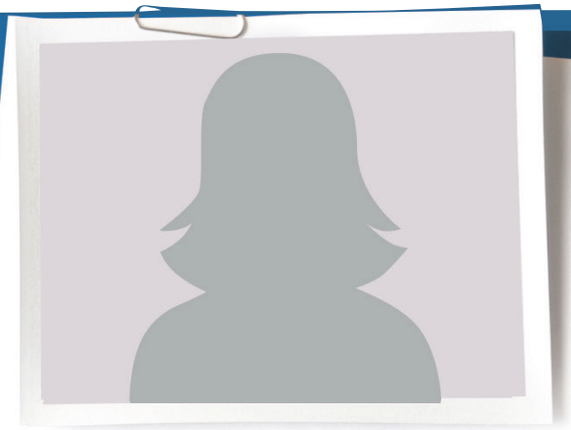
The physician was concerned about the patient's high morphine equivalent dose (MED) and ongoing depression. A conversation with a clinical pharmacist experienced in pain management at the workers' compensation carrier's PBM provided information on evidence-based opioid tapering techniques and streamlining of therapy. (See related article on page 30).

The physician followed the recommended steps, and over a six-month period reduced the patient's MED by 50 percent. Further tapering is needed along with a change in treatment regimen for the patient's depression, which is not responding well to medication alone.

TWO DIRECTIONS TO CONSIDER

The physician and patient are at a crossroads. If no adjunctive therapies are added to the patient's current drug therapy regimen, the MED will likely increase by 40 percent over five years.[67] If the payer approves use of alternative therapies such as cognitive behavior therapy, physical therapy and/or non-pharmacologic treatments like massage, acupuncture and chiropractic services, the possibility opens up for opioid therapy to be discontinued at some point and the patient to return to work.

In this typical example, the cost of drug therapy for pain management and depression is about $925 per month. Without alternative therapies to achieve further tapering, opioid therapy may



PATIENT X

Sex: F **Age:** 46

Diagnosis: Shoulder/Neck Strain With Radiating Pain & Depression

Drug Therapy Regimen Related to Pain and Depression

Medication	Dose & Frequency	Therapeutic Category	Concerns
Tramadol	50mg 4 per day	Short-acting opioid analgesic	Can cause seizures and may increase risk of serotonin syndrome when used with other serotonergic agents
Morphine Sulfate ER	30mg 5 per day	Long-acting opioid analgesic	Chronic use of high dose opioids may lead to opioid tolerance, opioid-induced abnormal pain sensitivity (hyperalgesia), immunosuppression, and hormonal abnormalities. Opioid use not recommended for neuropathic or radiating pain
Cyclobenzaprine	10mg 3 per day	Skeletal muscle relaxant	Long-term use of muscle relaxants are not recommended. They can cause strong side effects and many drug-drug interactions, including serotonin syndrome, especially when used with antidepressants. Consider baclofen or tizanidine which would not increase risk of serotonin syndrome.
Venlafaxine	100mg 2 per day for 30 day trial	Antidepressant, also used as a neuropathic coanalgesic	This drug was prescribed for a one-month trial which may not be long enough. There is a risk of serotonin syndrome when used with other serotonergic agents.
Fluoxetine	40mg 1 per day; Patient was not taking regularly	Antidepressant	Not recommended for neuropathic pain. There is a risk of serotonin syndrome when used with other serotonergic agents. Polypharmacy could be reduced by using a neuropathic antidepressant to treat both depression and pain.
Gabapentin	400mg 3 per day; Patient was not taking regularly	Anticonvulsant, also used as a neuropathic co-analgesic	Recommended target dose is 1800mg. Dose increase may improve pain control and allow reduction of opioid dose

PAIN MANAGEMENT & DEPRESSION
drug therapy can cost
$925*/mo.
*Based on Average Wholesale Price

Patient X Case Scenario

continue indefinitely. Costs will escalate as higher opioid doses are needed and additional drugs are prescribed to treat side effects. If the patient is unable to return to work, the total claim costs will be significantly higher.

COSTS VS. BENEFITS

The cost of adjunctive and alternative therapies will be higher than the current drug therapy costs, depending on what is needed. However, the new therapies are likely to be needed for a limited period of time. If successful, alternative therapies can open up the possibility of the patient discontinuing opioid therapy at some point and returning to work. This could significantly reduce the overall cost of the claim.

Each claim is unique and the circumstances must be considered on a case-by-case basis. There may be cases that can benefit from alternative therapies to supplement or replace traditional drug therapies.

PREVENTING CHRONIC OPIOID USE

FAST FOCUS

Chronic opioid therapy is preventable in many, but not all cases. To minimize opioid use, payers can work with their PBMs to develop pain management strategies that advocate for use of conservative therapies based on evidence-based guidelines.

If a prescriber does not write an opioid prescription, the patient cannot develop an opioid dependence. It is a simple concept, but opioids are too often prescribed in workers' compensation when non-opioid conservative therapies are indicated by evidence-based guidelines. Inappropriate prescribing can lead to chronic opioid therapy defined as opioid use beyond 90 days post injury.[68] Opioids have not been proven safe or effective for treating chronic pain.[69] Long-term opioid therapy is associated with extended disability, less successful outcomes and higher utilization of medical resources.[70,71,72,73]

Opioids are rarely indicated for many common injuries seen in workers' compensation such non-severe knee, leg, ankle, shoulder and some low back injuries that do not involve fractures or require surgery.[74]

EVIDENCE-BASED TREATMENT GUIDELINES

The case scenario on page 27 is typical of a workers' compensation drug regimen. Evidence-based opioid guidelines, such as those developed by the American College of Occupational and Environmental Medicine (ACOEM), ODG and others— recommend a holistic approach to pain management and limited and appropriate use of opioids, especially in the non-acute phase of injury. The guidelines place the focus of treatment on the injury, not the patient's pain. The treatment goal is to restore as much function as possible so the patient can return to activities of daily living and work. Pain relief is a tool that enables the patient to participate in treatment and recover.

Effective conservative treatment can eliminate or minimize pain and help the patient return to work in a timely manner. Payers can partner with PBMs to develop strategies to reduce reliance on opioid therapy and prevent chronic opioid therapy. PBMs can conduct educational outreach with prescribers on evidence-based treatment guidelines. Informed prescribers are more likely to implement a course of conservative treatment and utilize alternative therapies when indicated by the guidelines.

COPING WITH PAIN

Research shows that several factors can influence chronic pain:

- the presence of depression, anxiety, anger, substance abuse and other psychological conditions
- a social support system that includes family members and work dynamics
- the presence of litigation
- the patient's ability to continue working[75]

Prescribers should set realistic expectations with patients regarding pain relief and consider use of cognitive behavior therapy, physical and occupational therapy, massage, acupuncture, yoga, chiropractic care and other alternative therapies to help patients cope with the presence of some pain long-term.

GOOD COMMUNICATION CAN KEEP THERAPIES ON TRACK

Claims professionals should question the use of chronic opioid therapy in all non-cancer claims. They can open a dialog with prescribers to gain a better understanding of the goals and progress of prescribed therapies. Questions can include:

- **Q** What are the goals for this patient's therapy?
- **Q** What alternative, non-opioid and non-pharmacologic therapies have been tried? Physical and occupational therapy, massage, acupuncture and/or chiropractic therapy may be beneficial
- **Q** What is the expected duration of therapy?
- **Q** Is there an endpoint for use of opioids?
- **Q** How do you objectively monitor adherence and functional improvement?
- **Q** Do you utilize regular, periodic urine drug screening? If not, why not? If so, what do you do with the results?
- **Q** What does the screening of this patient reveal? Prescribers should be screening for psychiatric issues, substance abuse & risks for abuse/misuse
- **Q** How will you change therapy if you find problem behavior?

MORE INFO

American College of Occupational and Environmental Medicine

http://www.acoem.org/Guidelines_Opioids.aspx

Work Loss Data Institute, Official Disability Guidelines (ODG)

http://worklossdatainstitute.verioiponly.com

Past issues of *RxInformer* contain information related to this topic. We referenced the articles and issues here. Access them at www.healthesystems.com/rxinformer.

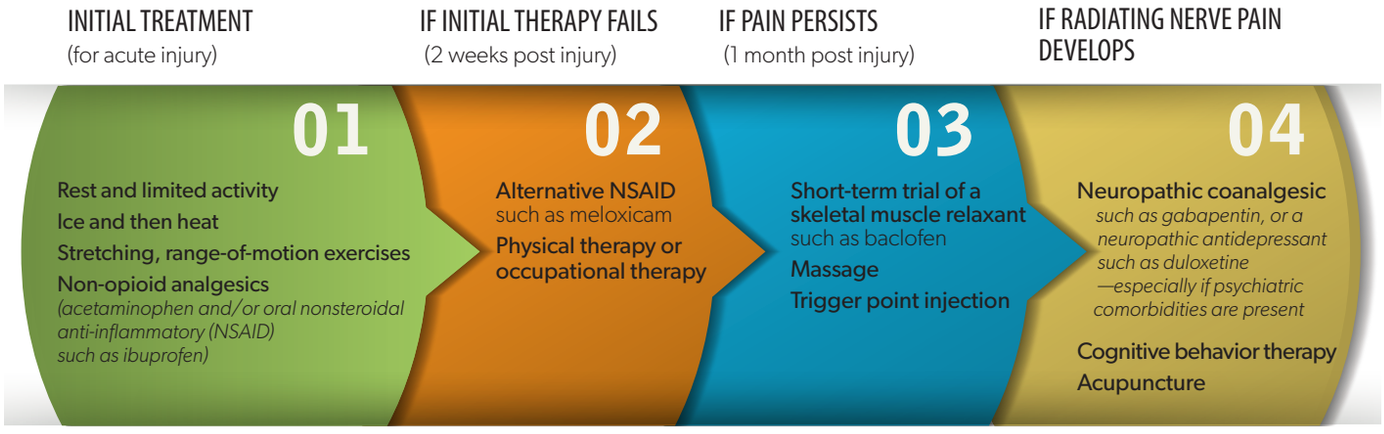
Opioid Therapy: Effective Case Planning, Fall 2013

Beyond Opioids: Alternative Pain Management Therapies, Fall 2013

THE BENEFITS OF A CONSERVATIVE APPROACH

A conservative approach to the neck and shoulder strain experienced by Patient X in the case scenario on page 27 would look very different and foster recovery instead of disability and opioid dependence.

The conservative regimen presented follows evidence-based guidelines and offers real potential for the patient to recover without opioid therapy.



COST CONSIDERATIONS

While the initial cost of treatment using a conservative approach might be higher than opioid therapy, payers can consider that the duration of these therapies is likely to be finite and result in the patient returning to work. A significant savings in overall claims costs can be realized and disability can be averted.

OPIOIDS: A GUIDE TO TAPERING & DISCONTINUATION

FAST FOCUS

Healthesystems clinicians reviewed evidence-based guidelines to assemble this reference for tapering and discontinuing opioid therapy.

Long-term opioid use often results in well-documented risks for the injured worker, payer and employer that include dependence, disability and high costs. In many cases, clinicians at a PBM can work with a prescriber to taper and discontinue opioid therapy and minimize or eliminate associated risks. There is limited evidence to support a specific rate of tapering or tapering protocol; however, best practices, recommendations and considerations were captured to create this resource.

TAPERING INDICATIONS

Patients may be ideal candidates for tapering off opioid therapy if:

1. The patient is taking high doses of opioids, regardless of whether they are long-acting or immediate-release formulations. Depending on the guidelines followed, high doses refer to daily morphine equivalent doses (MED) over 50-120. The 2014 opioid guideline developed by the American College of Occupational and Environmental Medicine (ACOEM) reflects the most current evidence and identifies 50 MED as the maximum recommended daily MED.

2. The patient shows no improvement in functional gains despite continued therapy.

3. The patient's pain has increased (hyperalgesia) or shows no modification despite dose increases.[76]

TAPERING CONSIDERATIONS

Discontinuation of opioid therapy is an intensely individualized process that depends largely on patient-specific factors. No single method of tapering works best, although all tapering protocols recommend against the abrupt discontinuation of opioid therapy. Here are some considerations to help make the tapering process as successful as possible.

TAPERING RATES

Tapering protocols range from a slow protocol of 10 percent per week for an injured worker without comorbid substance abuse or psychiatric disorders,[77] to a more rapid reduction of 25 to 50 percent every few days.

Anecdotal clinical evidence suggests that the initial dose reduction can be more rapid with high doses over 200mg of morphine equivalent per day.[78]

Once low daily doses are reached, a slower protocol may be required due to a higher incidence of withdrawal symptoms.

COMPREHENSIVE PAIN MANAGEMENT CENTERS

Reputable comprehensive pain management centers offer an option to effectively treat pain and reduce opioid use. They address the physical and psychological aspects of chronic opioid use using a team approach involving pain management and addiction specialists, psychologists, physical therapists and occupational therapists. Payers can look to the American Pain Society for a list of 35 clinics awarded its Clinical Center of Excellence in Pain Management designation. The designation signifies that each facility offers evidence-based, multidisciplinary, multimodal treatment.[83] These centers often provide a wide range of multidisciplinary services that may include yoga, biofeedback, acupuncture and chiropractor services, as well as vocational and work preparation programs. Success rates will vary, but one center reported that 70 percent of patients treated in 2010 returned to work within a year.[84]

For a list of centers recognized by the American Pain Society, visit http://tiny.cc/painmanagementcenter

WITHDRAWAL SYMPTOMS

Withdrawal from opioid analgesics is a potentially unpleasant experience. Symptoms often include:

gastrointestinal discomfort such as nausea, vomiting and diarrhea

muscle pain

runny nose

teary eyes

excessive salivation

insomnia

anxiety

sweating

increased blood pressure[79]

These symptoms should not be treated with opioids or benzodiazepines. Clinical studies indicate they are generally not life threatening and can be avoided or minimized with appropriate dose adjustments throughout the tapering process.[80]

COMORBIDTIES

It is vital that clinicians continue to treat patients withdrawing from chronic opioid therapy for pain and other comorbidities that may include substance abuse or psychiatric disorders. Pain management can be continued with NSAIDs, acetaminophen, neuropathic coanalgesics and topical agents such as lidocaine and capsaicin.[81]

ADJUNCTIVE THERAPIES

Non-pharmacological services can promote successful dose tapering. Referral to a mental health professional for cognitive behavior therapy (CBT) can assuage the anxiety that often accompanies the tapering process. Treatment with CBT to teach coping skills in support of the tapering process will not necessarily result in a psychiatric diagnosis. Therefore, other psychological services may not necessarily be compensable.

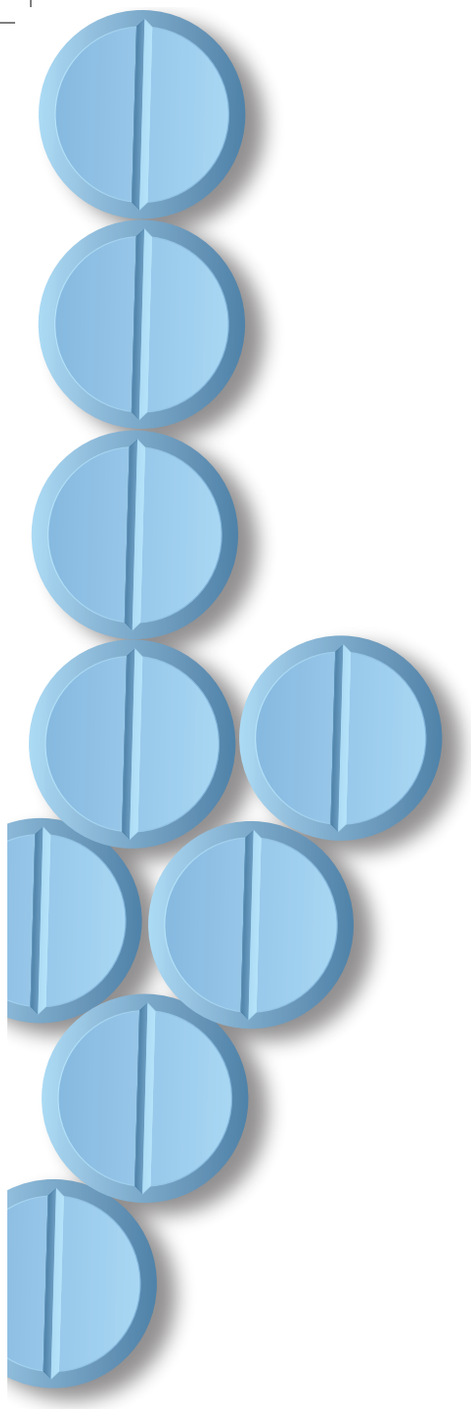
Aquatic and physical therapy are recommended to increase functionality and prevent muscle stiffness and pain.[82] Some patients can benefit from adding occupational therapy, vocational rehabilitation, massage, acupuncture and chiropractic services during tapering.

MONITORING

It is important to continually evaluate patients for comorbid conditions and mental disorders that could include depression and elevated risk for drug abuse or diversion.

REFERRALS

Consider referring high-risk patients to a multidisciplinary pain management center where tapering can be closely monitored. Patients with an opioid addiction may not be candidates for outpatient tapering and may require a referral to a detoxification program.



BEFORE TAPERING

Payer and prescribers can take a number of actions in advance of commencing a tapering protocol to increase the likelihood of success.

Payers can request a copy of several documents to gain a clear understanding of what is happening with the patient.

The physician's written treatment plan should reflect findings from a physical exam and provide a plan for starting and stopping opioid therapy. The treatment plan should consider the patient's mental state, functional abilities, activities of daily living, daily social and work activities as well as pain when creating realistic pain management goals.

A prescriber/patient pain management agreement outlines the goals of therapies and responsibilities of each party, and should include a stipulation for using a single prescriber and single pharmacy for pain medications

The physician's plan for opioid discontinuation should indicate the steps currently planned and a status on each if the plan is in progress.

Prescribers can reduce use of multiple drug therapies (polypharmacy) by streamlining the number of medications prescribed. This can reduce side effects and promote adherence to a medication regimen.

Prescribers can optimize alternative pain management strategies such as neuropathic agents, non-opioid analgesics, skeletal muscle relaxants and treatment for psychiatric comorbidities.

Prescribers can provide the patient and caregivers with instructions regarding the tapering process to minimize anxiety

MORE INFO

Healthesystems covered the topic of opioid therapy extensively in *RxInformer*. Select articles and issues are referenced and can be accessed at www.healthesystems.com/rxinformer.

Washington State Pain Management Guidelines, Fall 2013

Opioid Therapy: Effective Case Planning, Fall 2013

The Opioid Epidemic, Fall 2013

Beyond Opioids: Alternative Pain Management Therapies, Fall 2013

Red Flags in Opioid Therapy, Fall 2013

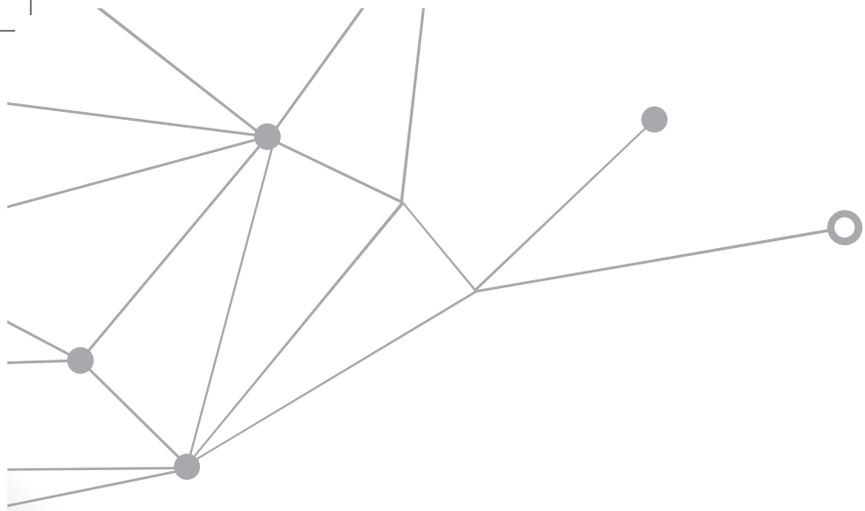
Risk Assessments in Opioid Therapy, Spring 2013

Know When to Stop Prescription Therapy, Spring 2012

UNDERSTANDING PAIN:

NEUROREMODELING

DOES CHRONIC PAIN HAVE TO BE CHRONIC?



FAST FOCUS

When acute trauma or injury changes nerves along pain pathways in the central nervous system, the brain's perception of pain can be altered, and the stage can be set for chronic pain. A number of therapies have proven useful in resetting the brain's perception of pain and curbing chronic pain.

Pain is a normal response by the body to prevent further damage and promote healing. While an uncomfortable sensation, it is generally a temporary phenomenon. Not all pain is bad. In fact, pain is part of the body's protective system. When trauma or injury occurs, neurons send signals to the brain to stop the activity causing the pain.

Pain perception involves a very complex system of multiple receptors, neurotransmitters and nerve pathways that process and transmit signals to the brain.[85] With such complexity comes many opportunities for transmission errors to occur. Often chronic pain results after trauma or injury cause miscommunication and alterations in the transmission and perception of pain. Studies prove that certain interventions can reset nerve pathways and lessen or eliminate some chronic pain.

A TYPICAL WORKERS' COMPENSATION INJURY

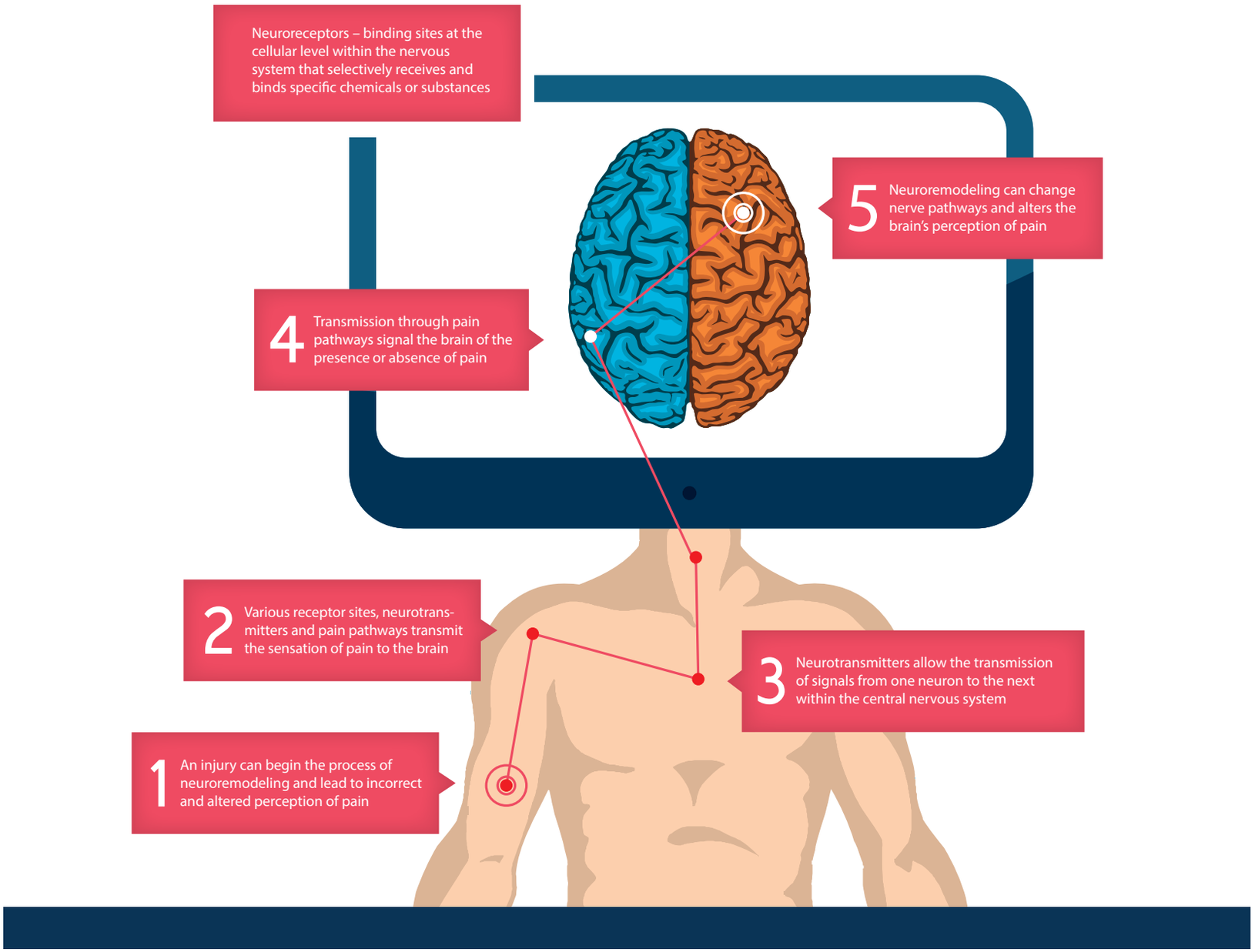
Consider a hypothetical case involving an office worker who lifts a heavy box and strains her neck and shoulder. The patient's pain would normally subside in about two weeks.[86] Evidence-based treatment guidelines call for acetaminophen or a nonsteroidal anti-inflammatory (NSAID) as first-line medications. However, a small group of patients may continue to experience prolonged or greater-than-anticipated pain relative to the severity of this injury. In those rare cases, treatment may progress to include other medications such as opioids. Prolonged acute pain and/or exposure to opioid therapy could begin to change the brain's perception of pain.

THE BRAIN ADAPTS

The brain's ability to adapt to changing circumstances is a factor. This innate ability — called neuroplasticity — occurs throughout a person's lifetime. It can result in the brain and pain transmission pathways becoming rewired — or neuroremodeled. When this occurs, nerves along the pain pathway may be altered, causing a maladaptive change in the patient's perception of pain. This maladaptation by the brain can complicate the rehabilitation of this patient and hinder her ability to return to work.

To understand the concept of neuroremodeling, think of the brain as a computer hard drive. The hard drive runs dozens of programs in the background in order to process and interpret constant inputs. A complex system of microchips and wiring transmits millions of pieces of information in the blink of an eye. If we boot up our computer and a critical file is corrupted or a key program misfires, the hard drive may not operate properly or may stop operating altogether. We may need to repair it or completely reboot it to get working again.

The same holds true of the brain, which continually processes and interprets inputs and generates outputs through the central nervous system. When neuroremodeling changes the nerves on the pain pathways, a breakdown in transmission of pain can occur and lead to unexpected outcomes. The brain can begin to perceive pain when no harmful stimuli are present or may heighten or mute the sensation of pain in response to stimuli. Repairing or rebooting the brain's processor may be in order.



OPIOID-INDUCED HYPERALGESIA

One example of a maladaptive neuroremodeling occurs when opioid receptors undergo an alteration of function. In certain patients, this may increase instead of decrease the sensation of pain when opioid therapy is administered. This effect is called opioid-induced hyperalgesia (OIH). In the case of a patient suffering from OIH, removing opioids from the system through a tapering and discontinuation process may cause a reboot, and reset the patient's perception of pain. A medically supervised gradual reduction is recommended and the assistance of a comprehensive pain management center may be indicated. Pharmacologic treatment — particularly opioid treatment — may be ineffective in treating pain for these patients so alternatives may need to be considered. [See related article, page 28 Preventing chronic opioid use]

REVERSING NEUROREMODELING

A number of treatment options can lessen chronic pain by reversing the misalignment of pathways that affect the way the brain processes pain. Options for reversal of this neuroremodeling include opioid tapering and discontinuation, mirror therapy, biofeedback and cognitive behavior therapy.

MIRROR THERAPY

A well recognized example of a mind-over-matter approach to changing the brain's perception of pain is mirror therapy. Mirror therapy has been used successfully to treat phantom limb pain often experienced by amputees. It involves showing the amputee a reflected image of an intact limb repeatedly over a defined

period of time. The brain begins to "see" an intact limb instead of perceiving a missing limb. The sensation and pain associated with the missing limb is reduced or eliminated. One study looked at the effects seen in the brain pre- and post- mirror therapy and documented the successful reversal of neuroremodeling and decrease in phantom pain.[87]

PSYCHOTHERAPEUTIC INTERVENTIONS

Interventions such as biofeedback and cognitive behavior therapy (CBT) also work on the brain's perception of pain and may be useful in reversing the remodeling process. Biofeedback achieves this by creating greater awareness of the patient's physiologic expressions of pain in their own body so they can manipulate and control them to alter their perception of pain or keep pain from escalating. Patients can be taught to change their thoughts and control emotions, which can result in improved breathing patterns, slowed heartbeats, lowered blood pressure and a reduced perception of pain.

Cognitive behavior therapy (CBT) addresses the relationship of cognitive factors to pain behaviors. Through CBT, a patient can learn to identify their own negative, habitual thoughts related to pain and recognize the connection between their pain and those thoughts and resulting feelings. The perception of pain may be minimized by teaching the patient to substitute more adaptive thoughts and use coping strategies such as relaxation, distraction, imagery and self-hypnosis. [88]

ALTERNATIVE THERAPIES GAINING GROUND IN COMP

While not widely utilized in the work comp environment, these therapies are gaining ground and are increasingly included in treatment guidelines. The 2013 updates to Delaware Department of Labor Healthcare Practice Guidelines support the use of these modalities in the plan to improve care to the injured worker.[89] The state of Washington also updated treatment guidelines in 2013 to include recommendations for cognitive behavior therapy in the treatment of pain.[90]

Interventions such as CBT are only beginning to gain ground in the treatment of pain, but CBT is widely recognized in the treatment of addiction. According to SAMHSA, in 2010, approximately 66 percent of addiction treatment centers reported using CBT as part of the comprehensive plan.[91] Consider that early intervention with alternative therapies may improve patient care, prevent development of chronic pain and reduce costs associated with long-term claims.

FINANCIAL CONSIDERATIONS

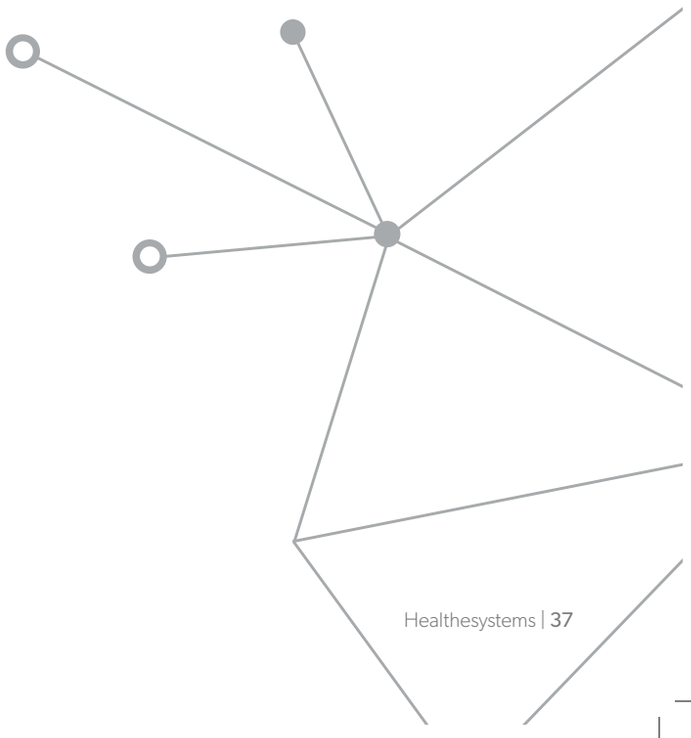
As more states revise opioid guidelines, alternative therapies will need to be given serious consideration. The costs of these therapies may initially appear excessive when compared to the cost of medications; however, the potential long-term benefits of reducing opioids and other medications and preventing chronic pain must be weighed.

MORE INFO

Healthesystems covered the topics of opioid and alternative therapies extensively in previous issues of *RxInformer*. Select articles and issues are referenced and can be accessed at www.healthesystems.com/rxinformer.

Opioid Therapy: Effective Case Planning, Fall 2013

Beyond Opioids: Alternative Pain Management Therapies, Fall 2013



ZOHYDRO ER: PROCEED WITH CAUTION

FAST FOCUS

Controversy surrounded the FDA approval of Zohydro ER™ due to safety concerns. This powerful, long-acting new opioid lacks abuse-deterrent properties and is now on the market. Its use should be discouraged.

Zohydro ER™ (hydrocodone bitartrate extended-release capsules) received FDA approval in October 2013, for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment, for which alternative treatment options are inadequate.[92] It is the first formulation of hydrocodone as a single entity — meaning it is not combined with an analgesic such as acetaminophen — and the first extended-release hydrocodone formulation. Zohydro is in the same high-risk category as other opioid products such as OxyContin® (oxycodone extended-release tablet) and Exalgo® (hydromorphone extended-release tablet). However, unlike other extended-release opioids, Zohydro ER is not abuse-deterrent and has the potential to be crushed easily or chewed.

CONTROVERSIAL APPROVAL

FDA approval came despite an 11-2 vote against approval by the FDA's own scientific advisory panel. Due to several safety concerns, attorneys general from 28 states and more than 40 different groups and experts requested the FDA to reconsider Zohydro's approval.[93,94] Subsequently, six other attorneys general joined in asking for approval to be reversed with a letter to the Department of Health and Human Services.[95]

The FDA approval was based on a 12-week study in patients with moderate-to-severe chronic lower back pain. Therefore, in addition to the safety concerns, it is unclear whether the results can be generalized to long-term opioid therapy for which the drug is approved.[96]

ABUSE POTENTIAL

In November 2013, the FDA staff issued a memo warning that Zohydro is expected to be abused more than traditional hydrocodone combination products.[97] These safety concerns exist largely because Zohydro is an extended-release opioid formulation without abuse-deterrent properties. Tampering with an extended-release delivery system can lead to uncontrolled and rapid delivery of the entire contents of the product. This provides the user with a "high" and increases the likelihood for overdose and death.[98]

Because of these risks, attorneys general also called for a rigorous timeline for development of an abuse-deterrent formulation in their letter to the FDA.[99] Meanwhile, in order to comply with FDA requirements aimed at reducing the risks for misuse, abuse, addiction, overdose and death associated with all extended-release and long-acting opioid analgesics,

Zohydro's labeling must emphasize appropriate patient selection and warn that serious safety risks exist even at recommended doses.[100]

In response to these safety concerns, Zogenix is developing an abuse-deterrent Zohydro formulation that is expected to reach the market in 2017.[101] The new formulation will use a delivery system called Intellitab™, advertised as ultra-hard to resist crushing and chewing, and resistant to dissolution in alcohol.[102] According to the manufacturer, crushing and adding an Intellitab formulation to a liquid produces a hard, dry matrix that avoids dose dumping and the desired "high." However, loopholes exist even with purported abuse-deterrent formulations, as indicated by a study which concluded that 24 percent of Oxycontin abusers found a way to overcome the formulation's abuse-deterrent safety measures.[103]

USE IN WORKERS' COMPENSATION

Extended-release or long-acting opioids are prevalent in workers' compensation. Zohydro is expected to be prescribed for patients requiring chronic pain management, similar to what is seen with other extended-release or long-acting opioids which are prevalent in workers' compensation. However, its use should be discouraged. While select patients may benefit from Zohydro, the risks for addiction, abuse and diversion must be carefully balanced with the expected benefits on a patient-by-patient basis.

Though Zohydro is less potent than other opioids such as Opana and Oxycontin, and may represent an appropriate step down in therapy, the lack of abuse-deterrent properties may lead certain patients to request Zohydro over other long-acting opioids. Therefore, the appropriateness and clinical rationale for choosing Zohydro should be confirmed for each patient.

Zohydro is designated as an "N" drug by the Official Disability Guidelines (ODG) and will require prior authorization in states that have adopted ODG Treatment Guidelines as mandatory. All payers are urged to require prior authorization for Zohydro and encourage prescribers to maximize use of non-opioid analgesics first.

Zohydro ER is available in 10mg, 15mg, 20mg, 30mg, 40mg, and 50mg capsules for twice daily administration. Due to the increased abuse potential, Zohydro is a Schedule II substance. Therefore, it will require a new written prescription each time the medication is needed, as refills are not allowed for Schedule II substances.

LEGISLATIVE ALERT

US HOUSE & SENATE SEEK TO BAN ZOHYDRO

In mid-March, bills were introduced in the House of Representatives and Senate to compel the FDA to withdraw approval of Zohydro ER. If passed as submitted, the bills would further prohibit the FDA from approving such a drug in a formulation that is not abuse deterrent.

MA BANS ZOHYDRO

The Governor of Massachusetts recently declared a public health emergency in response to the state's growing opioid epidemic and initated a ban on prescribing and dispensing any hydrocodone-only formulation until it has been determined that adequate safeguards are in place.

VOTE by the FDA Scientific Advisory Panel
AGAINST APPROVAL OF **ZOHYDRO**

STATE ATTORNEYS GENERAL
requested **reversal of FDA approval of Zohydro.***
** As of March 25, 2014*

MORE INFO

Healthesystems has written about related topics in the past. Select articles and *RxInformer* issues are referenced and can be accessed at www.healthesystems.com/rxinformer.

Hydrocodone: Use, Abuse & Controls, Spring 2013

New Opioids Require Close Scrutiny, Spring 2012

Reformulated Opioids: Are Abuse Deterrents Losing Their Promise? Spring 2012

Hydrocodone: Use, Abuse and Controls on Prescribing,

Abuse-Deterrent Opioids, Fall 2010

FDA ACTIONS ADDRESS **ACETAMINOPHEN TOXICITY** RISKS

FAST FOCUS

The FDA recognized the risks of high doses of acetaminophen by asking prescription drug manufacturers to lower the maximum content per pill or capsule by January 2014. The request did not apply to over-the-counter preparations, so risks will remain until all the supplies of all high-content formulations are depleted.

In high doses, acetaminophen can cause toxicity and lead to serious liver damage or even death. In 2011, the National Council for Prescription Drug Programs (NCPDP), FDA and other interested parties focused attention on patient safety issues with the formation of the Acetaminophen Best Practices Task Group.[104]

To minimize patient risks, the FDA asked prescription drug manufacturers to limit acetaminophen content to a maximum of 325mg per tablet or capsule by January 1, 2014.[105] The high dose acetaminophen products seen most frequently in workers' compensation are Vicodin®HP, Vicodin® ES, Percocet® products, Lortab® and their generic versions.

In response to the FDA request, many manufacturers reformulated their products and received FDA approval for reduced acetaminophen content. Brand names were retained and a few products were discontinued. Generic manufacturers also complied with the request. As a result, there should be no impact on the use of generic products as substitutes for brand-name prescriptions with the lower acetaminophen dose.

The FDA made a provision for manufacturers and retailers to deplete existing supplies. Since they were permitted to continue manufacturing the higher dose products until the 2014 deadline, higher dose products remain on the market. Until supplies of the higher strength products are depleted, patients remain at higher risk for excessive use. This is especially true for patients who may take over-the-counter (OTC) formulations and prescription preparations containing acetaminophen since the FDA request did not apply to OTC.

ENHANCED PATIENT SAFETY

The FDA is urging prescribers to use the lower dose formulations even if the older formulations are still available.[106] Encouraging prescribers to reduce acetaminophen use and educate patients remains important in curbing patient risks. The limits placed on one source of acetaminophen and the increased awareness of patients, prescribers and insurers of the risks of taking too much should improve patient safety.

Healthesystems saw a **63% decrease in acetaminophen** prescriptions containing **> 2600 mg daily** between 2012 and 2013. It is possible that all the attention being focused on the risks, combined with strategic intervention, is having a positive effect.

SAFE MEDICATION USE

Patient education is one of the key factors that influence safe medication use. All parties involved in patient care need to help patients understand which products contain acetaminophen and the daily use limits. Patients should be expected to keep track of all medical products they are using, both prescription and OTC, and total up daily acetaminophen milligrams to avoid overuse. The FDA website has a wealth of information for patients.[107]

AVOIDING ACETAMINOPHEN TOXICITY

1. **Read labels of all over-the-counter and prescription drug products to identify acetaminophen content**
2. **Ask prescribers or pharmacists to identify acetaminophen in products when talking to patients**
3. **Know the limits of daily acetaminophen doses from all sources**
4. **4000 mg daily for short-term use (a few days)**
5. **2600 mg daily for regular use**
6. **2000 mg daily if kidney function is low as in patients on dialysis or with severe kidney damage**
7. **Avoid use if liver function is poor**
8. **Avoid use with alcohol**
9. **If possible, avoid use of more than one product containing acetaminophen**

Regardless of the actions taken to protect patients, acetaminophen use remains a concern. Thousands of prescription and over-the-counter products contain this useful drug. All healthcare providers need to be alert to the presence of this common drug and help patients limit use to safe doses.

FDA LABELING CHANGES FOR OTC PRODUCTS

Over-the-counter (OTC) products were not included in the FDA's reformulation request though labeling changes were requested.[108] Many consumers are not aware of the amount of acetaminophen contained in products. Even worse, consumers may not have realized acetaminophen was even present. Acetaminophen is a common ingredient in sleep aids and products made to treat general pain, coughs and colds, headaches and menstrual cramps.

Labeling changes requested to improve over-the-counter product identification included:[109]

- Clearly identify acetaminophen as an ingredient
- Include new warning about liver toxicity
- Include a warning that other products containing acetaminophen should not be used together

LOOK FOR ACETAMINOPHEN ON THE LABEL

Here is an example of how easy it is to exceed the recommended daily dose of acetaminophen. This patient is taking a prescription analgesic, cold medication and sleep aid. All contain acetaminophen.

Total Daily Acetaminophen Dose = 5,050mg

TOP 5
ACETAMINOPHEN PREPARATIONS IN WORKERS' COMPENSATION*

Product	Acetaminophen Content Before Change	Acetaminophen Content After Change	Generics Available?
Vicodin HP	660mg	300mg	Yes
Vicodin ES	750mg	300mg	Yes
Percocet family of products	325mg up to 650mg	All now 325mg	Yes
Lortab	500mg	Product discontinued	N/A
Lorcet, Lorcet Plus	650mg	Products discontinued	N/A

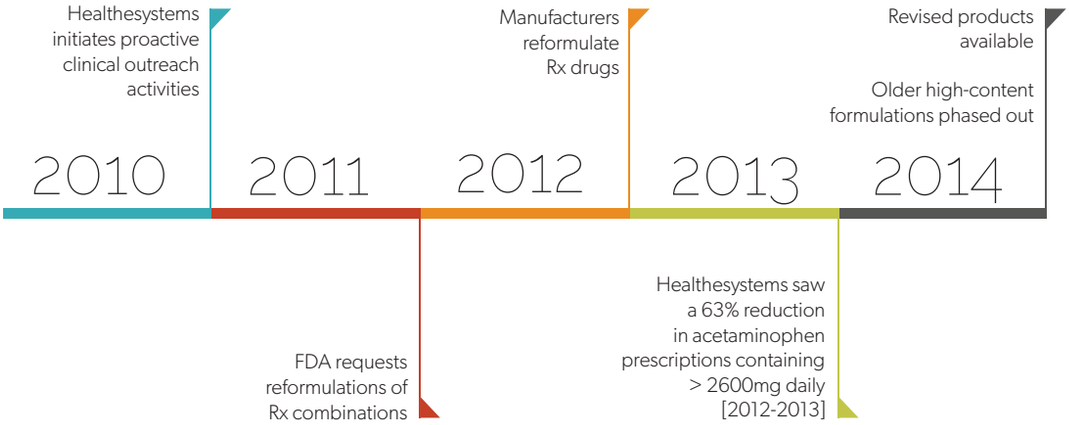
*Based on a Healthesystems clinical analysis.

MANY FACTORS INFLUENCE ACETAMINOPHEN RISKS

A number of factors can escalate a patient' risks for acetaminophen toxicity. They include excessive daily doses, concurrent alcohol consumption, diminished liver function, concurrent use of over-the-counter medications containing acetaminophen, kidney disease and smoking.

Healthesystems' ongoing clinical outreach program alerts payers and prescribers to these risks and provides an opportunity for intervention to reduce the risks. This program was in place even before the FDA made its request to pharmaceutical manufacturers for a reduction in per pill and per capsule content. Excessive acetaminophen use is too important an issue to ignore. The risks are of liver damage and liver failure are serious and potentially fatal. The loss of even one life and the need for a single liver transplant are too high a price to pay.

ACETAMINOPHEN NEWSWORTHY HIGHLIGHTS



TOP CHALLENGES OF MANAGING ANCILLARY MEDICAL BENEFITS

FAST FOCUS

Unique issues related to coding, processing and program management make it difficult for payers to know exactly what ancillary medical products and services are provided to injured workers and at what price.

It can be especially challenging for workers' compensation payers to control and manage ancillary medical services. Unique issues related to coding, processing and program management make it difficult for payers to know exactly what products and services are provided to injured workers and at what price.

Payers often do not have a clear understanding of how much is spent for durable medical equipment, home health, transportation, translation and language services due to lack of detailed codification. Transportation services are a good example. Many payers use inconsistent methods to capture transportation billing. Some claims professionals may authorize bill payments off the claim as an expense, while others will send bills through bill review.

CONTROL STARTS WITH DETAILED CODING

If a payer is able to identify spending in each service category, the next challenge is to understand exactly what services and products are provided in that category and at what price. Codes for services are often applied inconsistently. Many are billed with a miscellaneous code; others may be billed using different codes for the same type of service. When ancillary medical services are paid in bill review, confusion frequently contributes to between one-third and one-half of bills being denied — often due to bill duplication, lack of relationship to the claim and lack of prior authorization. When product-specific codes and detailed descriptions are applied on referrals and bills, payers gain a clear understanding of the products and services delivered and the price charged for each.

TOP ABM CHALLENGES

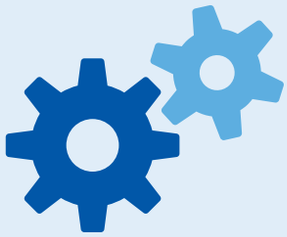
CODING

Lack of transparency

No product-specific codes & descriptions

No defined units of measure

Use of miscellaneous codes



PROCESSES

Bill disputes

Overutilization

Wasted time

Increased costs

Referrals, authorizations & billing not integrated

Lack of proper authorizations

PROGRAM MANAGEMENT

No mechanisms to measure vendor performance

No control over utilization, costs & quality

No process improvement

LACK OF DETAILED CODING CAN BE COSTLY

Mileage charges related to transportation services are often billed under code A0425, regardless of the type of transportation provided. Use of detailed coding gives payers greater transparency.

	Cost Per Mile
Advanced Life Support Transport	$$$$$$$$$$
Basic Life Support Transport	$$$$$$$$
Stretcher Transport	$$$$$
Wheelchair Transport	$$$
Ambulatory Transport	$

INTEGRATED PROCESSES REDUCE COSTS

The second set of challenges are related to processes involved with referrals, authorizations and billing. When these processes are clearly defined and integrated with one another, the correct services and products can be delivered at the right time and at the correct price. Ancillary medical services delivered outside of an integrated and fully managed program often lack proper authorization. This can lead to bill disputes, overutilization, wasted time and increased costs. When prior authorizations are linked systematically to bill processing and payment, payers gain control over utilization and costs. This process also eliminates overpayments and underpayments.

PROGRAM MANAGEMENT ENSURES QUALITY AND EFFICIENCY

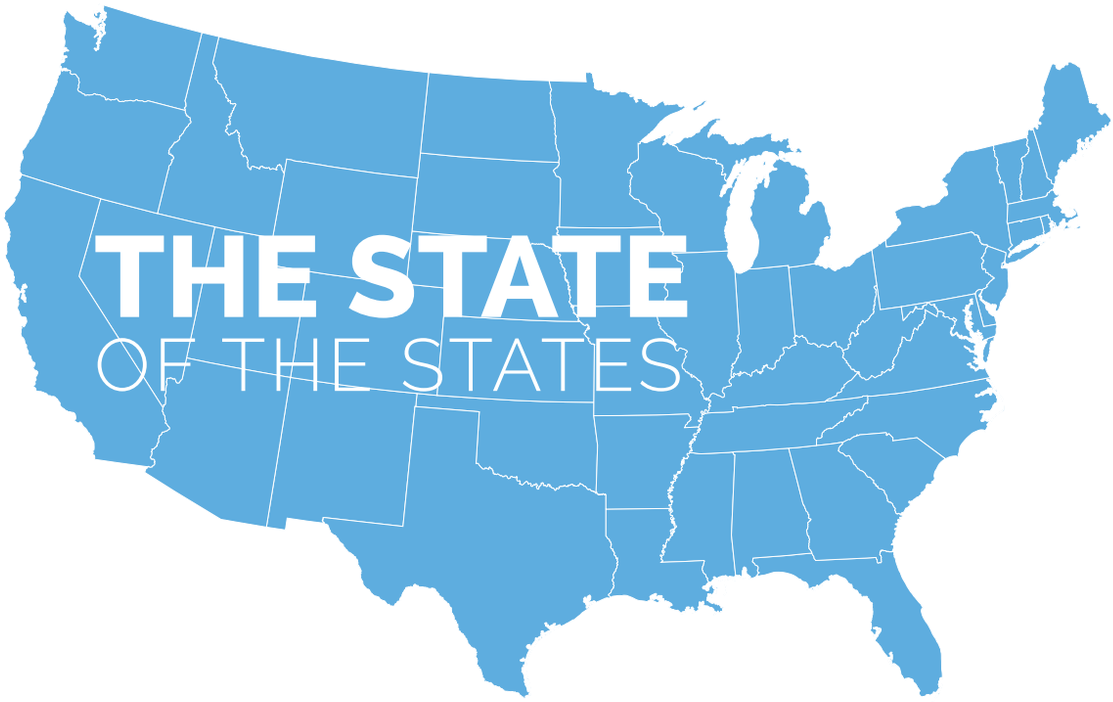
Even when coding and billing is accurate and utilization is well controlled, payers face the challenge of maintaining quality and evaluating the performance of individual vendors as well as the overall program. Metrics can be established for every vendor and every aspect of an ancillary benefit program. Analytics can evaluate performance across like vendors and serve as a blueprint for process improvements if needed. Payers can use hard data to determine if a change of vendors may be needed. The more aspects of quality and performance that are measured, the more control payers can have over utilization, quality and costs of ancillary medical benefits.

MORE INFO

Healthesystems covered the topic of ancillary medical benefits in past issues of *RxInformer*. Select articles and issues are referenced and can be accessed at www.healthesystems.com/rxinformer.

Bringing Visibility to Hidden Home Health Costs, Fall 2013

Electrotherapy: Identifying Drivers to Manage Costs, Fall 2011



OKLAHOMA
Closed Formulary Adopted

After monitoring the positive impact of Texas' closed formulary, Oklahoma adopted its own with some differences.

The Oklahoma formulary is effective for claims arising on or after February 1, 2014, so there will be no legacy claims to transition into the requirements.

While there are similarities between the two states' closed formularies, the Oklahoma exclusions are broader than Texas'. Both Texas and Oklahoma exclude any drug in the Official Disability Guidelines "N" Drug List and all experimental and investigational drugs. The Oklahoma formulary excludes all compounds, while the Texas formulary only excludes those that contain "N" drugs. In addition, the Oklahoma formulary excludes all drugs that are not preferred, exceed or are not addressed by the ODG in effect on the date of treatment. Any drug not included in the formulary requires preauthorization.

Once a provider makes a preauthorization request, the carrier or employer must respond within 72 hours or the preauthorization request is granted. If the provider prescribes a drug that requires a preauthorization request but failed to obtain preauthorization, the payer may deny payment for that drug.

Changes and challenges might be lodged with the implementation as the number of claims affected by the closed formulary increases because it was developed using an abbreviated timeframe, giving stakeholders less time to provide feedback.

OHIO
Reimbursement Limits for Non-Sterile Compounds

The Ohio Bureau of Workers' Compensation adopted revisions to the rule, Payment for Outpatient Medications by Self-Insuring Employer, OAC 4123-6-21.1, effective December 1, 2013. The revisions establish a payment methodology limiting reimbursement for non-sterile compounded prescriptions. Previously, the reimbursement formula for pharmacy providers included both a product cost component and a dispensing fee component. The rule change adds two elements to the product cost component for compound drugs. First, the product cost component for non-sterile compounded prescriptions is now limited to the lesser of the usual and customary price or the average wholesale price of the commonly stocked package size minus 9 percent for each ingredient. Secondly, the maximum product cost component reimbursement for any one non-sterile compounded prescription is $600.

The dispensing fees for compounded prescriptions, payable only to pharmacists, remain unchanged at $12.50 for non-sterile compounds and $25 for sterile compounds.

NEW YORK

Prescription Drug Monitoring Program Commended

New York Attorney General Eric T. Schneiderman applauded the release of data documenting the success of the state's program to prevent prescription drug abuse, the Internet System for Tracking Over-Prescribing Act, known as I-STOP. The I-STOP program implemented a real-time database in August 2013. Physicians are required to consult it before writing prescriptions for Schedule II, III or IV controlled substances. Pharmacists are required to report in real time each time they fill a prescription for Schedules II, III, IV or V drugs. They are also required to consult the database before filling such prescriptions. New data shows that more than 66,000 New York health care professionals have queried the database on more than 7,000,000 individual prescription checks on nearly 3,000,000 different patients since inception.

The I-STOP program is credited with helping prescribers avoid dangerous drug interactions and detect drug abusers using pharmacies as suppliers. New York is expecting additional progress in the fight against prescription drug abuse in March 2015, when I-STOP mandates e-prescribing for all drugs, a move the state believes will eliminate the current problem of forged, traded or stolen prescriptions. More information on I-STOP is available on the New York Attorney General's website www.ag.ny.gov/feature/i-stop.

KENTUCKY

Fee Schedule Proposal Will Address Repackaged Drugs

The Kentucky Department of Workers' Claims (DWC) is proposing fee schedule changes that will replace the current 2010 fee schedule. Pursuant to KRS 341.035, the department is required to review and update the schedule of fees, if appropriate, every two years. Several significant changes are being proposed to the Workers' Compensation Schedule of Fees, including clarification language that will address repackaging of medications in a physician's office.

The proposed language states, "If a drug is repackaged by a physician, the average wholesale price is determined using the National Drug Code (NDC) of the original product from the manufacturer. The physician shall include the NDC from original manufacturer with the invoice. Invoices that do not include the NDC of the original product may be returned to physician as incomplete." This new regulation will allow for the continued practice of physician dispensing but at prices comparable to those charged by pharmacies.

Healthesystems attended a public hearing on February 25, 2014, at the offices of the Department of Workers' Claims. The DWC accepted written comments until February 28, 2014. The DWC has reviewed the written and verbal comments submitted by interested stakeholders and posted responses on its website. The proposed changes can be viewed on the Department's website http://tiny.cc/workersclaims

MICHIGAN
Regulation of Compounds and Opioids

The Michigan Workers' Compensation Health Care Services (HCS) Advisory Committee is developing rules to establish a reimbursement methodology for compound drugs. The current draft would allow reimbursement of compounds upon preauthorization by the carrier or employer. The draft rule requires the prescriber to demonstrate the effectiveness and safety of the compound through peer-reviewed medical and scientific literature. Active component ingredients of the compound must have NDC numbers and must be FDA-approved drugs that have not been withdrawn or removed from the market for safety reasons. Compound drugs will be billed by listing the quantity of each component drug and its NDC number. Reimbursement will be based on the total of AWP minus 10 percent of each ingredient, plus the cost of the inert ingredients at manufacturer's original invoice cost, as well as a single dispense fee of $5.50.

In its current format, the rule will be difficult to implement. Information supporting the automation of a process to identify a compound drug ingredient as inert may not be readily available in drug pricing databases, therefore changes may be expected before the rule is finalized.

The HCS Advisory Committee is also drafting rules to regulate the use and reimbursement of opioids for chronic, non-cancer pain. The current draft links physician reimbursement to compliance with treatment parameters, and requires reimbursement for opioids for chronic pain when the medication is medically necessary. To receive reimbursement for opioid treatment of pain, physicians would be required to submit a written report to the insurer no later than 90 days after the initial opioid prescription fill for chronic pain, and every 90 days thereafter. Draft rules specify the content of the report, inclusive of such requirements as mandatory urine drug screening, an opioid contract signed by the injured worker and the attending physician, review of data from the Michigan Automated Prescription System (MAPS) and consideration of weaning the patient from opioids. The rule would also permit physicians to bill for additional services associated with complying with the rule, including a $25 charge for accessing the MAPS database.

A potential obstacle to the implementation of both the compound and opioid rules is Michigan, which law, does not currently support a prospective utilization review process. Healthesystems is working with interested stakeholders and provided feedback relating to both rules to HCS Advisory Committee members.

TEXAS
2014 Prescription Drug Studies

The Texas House of Representatives and the Texas Division of Worker's Compensation (DWC) released lists of studies they would like to complete before the next legislative session convenes in January 2015. Items to be studied include the state's closed drug formulary, medical costs and utilization, and prescription drug use.

Closed Formulary – The Division of Worker's Compensation will study the impact of the state's closed drug formulary on utilization and cost patterns in pharmacy prescriptions and conduct an annual update of medical costs and utilization in the Texas workers' compensation system. Both studies are required by state law.

Prescription Drug Use – The Texas House Committee on Public Health will study the prevalence of the use of prescription drugs, such as opioids for non-medical use, and make recommendations for steps that can be taken to limit this form of drug abuse. Another study will look for recommendations on how the system of licensing, regulation and monitoring of compounding pharmacies can be improved. The committee will also review the joint work conducted by the Texas Board of Pharmacy, Department of State Health Services and the U.S. Food and Drug Administration related to compounds. In addition, it will review the impact of a law passed in 2013 to license and inspect out-of-state pharmacies that create sterile compound drugs, a measure filed in response to the 2012 outbreak of fungal meningitis resulting from tainted injections from a compounding pharmacy in Massachusetts. The current system for dispensing biologics (drugs synthesized from living organisms or their products) and biosimilars (highly similar versions of other biologics, also known as follow-on biologics) will also be studied. Recommendations will be made on how biologics and biosimilars may be substituted for each other or for chemical drugs.

MISSISSIPPI

Reimbursement Cap Adopted on Compound Creams

State regulators are seeking ways to control the rising costs of compound drugs dispensed to injured workers. With use increasing, the Mississippi Workers' Compensation Commission (MWCC) adopted a rule for compound cream medication as part of their Medical Fee Schedule update, effective November 1, 2013. The rule caps reimbursement for compound creams to $300 for 120 grams per month. Doctors would have to supply additional documentation and obtain preauthorization for anything over the 120-gram limit. The commission felt that limiting reimbursement on compound creams would help curb costs since the price being charged by drug compounding companies and doctors for topical creams prescribed to treat pain is very high. The medical fee schedule is not available on the Commission's website but can be ordered through optumcoding.com (keyword: Mississippi Workers' Comp)

IDAHO

PDMP Use Required For Controlled Substances

House Bill 396 was filed to require prescribers of controlled substances, except veterinarians, to annually register with the Idaho Board of Pharmacy to obtain online access to the controlled substances prescriptions database, the state's prescription drug monitoring program (PDMP). The bill was signed by the governor on March 14, 2014. The law will become effective on July 1, 2014. The full text of HB 396 can be viewed on the Legislature's website, www.legislature.idaho.gov/legislation/2014/H0396.htm.

INDIANA

New Restrictions on Physician Dispensing

Indiana Senate Bill 294, filed on January 8, 2014, will amend the workers' compensation law that currently limits reimbursement of repackaged drugs to prevent physicians from dispensing drugs from the eighth day of injury onward. The bill will also add new provisions to the law that will limit reimbursement to a medical service provider to no more than one office visit for each repackaged drug prescribed. The bill passed both houses of the legislature and has been signed by the governor. It will become effective July 1, 2014.

BY THE NUMBERS

MEDICAL MARIJUANA

20 20 states and the District of Columbia have **LEGALIZED medical use of marijuana**

17 states have legislation under consideration to LEGALIZE MEDICAL USE OF MARIJUANA

STEP THERAPY

81% savings

$$$ AVG. SAVINGS achieved in a **step therapy** program for a targeted NSAID

ACETAMINOPHEN

↑MORE THAN

OVER-THE-COUNTER & PRESCRIPTION MEDICINES CONTAIN **ACETAMINOPHEN** INCLUDING MANY FOR COLD AND FLU SYMPTOMS

SOURCE: WWW.KNOWYOURDOSE.ORG

ER VISITS annually for **unintentional overdoses** OF ACETAMINOPHEN-containing products.

SOURCE: AMERICAN JOURNAL OF PREVENTIVE MEDICINE, 2011

SPECIALTY PHARMACY

Specialty pharmacy spending is expected to **INCREASE** from

SOURCE:IMS INSTITUTE FOER HEALTHCARE INFORMATICS: THE GLOBAL USE OF MEDICINES: OUTLOOK THROUGH 2017

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