myMatrixx®
An Express Scripts Company

2018

Workers' Compensation

Drug Trend Report

What's next for workers' compensation pharmacy?

In 2018, the industry and myMatrixx saw some exciting changes. Egregiously priced compounds are now almost nonexistent for most of our workers' compensation payers. Opioids have dropped to second place on the list of most commonly dispensed drugs for many payers. Prescription drug monitoring programs (PDMPs) now exist in all 50 states. More states than ever have adopted treatment guidelines and/or formularies. And advances in pharmaceutical science hold promise for a safer drug therapy future.

In spite of these positive advances, many of our clients are asking what's next? They worry that other drugs or conditions could have a similar effect on our industry and the lives of our injured workers as opioids. There's also significant concern over the rising cost of prescription drugs. Finally, there is a lack of understanding about the impact specialty medications may have on workers' compensation insurance.

On average, payers spent $5,130.57 per injured worker on a specialty medication. Specialty medications cost four times as much as traditional medications for payers. The maxim that the most expensive specialty drug is the one not taken means that poor adherence on the part of the patient may render even the best therapy ineffective. As an Express Scripts company, myMatrixx works closely with Accredo, the largest specialty distribution pharmacy network in the nation. Whenever possible, we recommend that injured patients receiving specialty drugs use the pharmacy services at Accredo where more than 500 pharmacists are devoted to patient care.

We address rising specialty costs and more in our 2018 Workers' Compensation Drug Trend Report. For the first time, our report combines both Express Scripts and myMatrixx data providing a more comprehensive view of the industry than ever before. In addition, we've enhanced our Get Ahead of the Claim program that has steered our clinical strategy for the past decade.

We're transitioning from an opioid-dominated management program to a pharmacovigilance program with even greater focus on other drugs of concern. This new program monitors and combats excessively priced drugs, identifies potential fraud and abuse, and has been a key factor in our 2018 results as we focus on avoiding the next possible crisis.

We've made some important changes to our methodology that reflect our changing marketplace. First, days' supply as opposed to number of prescriptions is used to measure prescription counts. This subtle change allows us to capture the changing dynamics in the marketplace as more restrictions are placed on quantities of dangerous drugs; prescription count may be artificially inflated. In addition, we have excluded specialty medications from the overall trend, reporting on the majority of payer pharmaceutical cost.

Lastly, please continue to join me in future broadcasts of Facetime with Phil as we delve further into the story behind the numbers and provide additional detail on the factors introduced and discussed in this year's report.

Phil Walls, RPh
Chief Clinical Officer
myMatrixx, an Express Scripts company

Driving down both drug utilization and spending for workers' compensation plans

In 2018, U.S. **drug spending decreased 3.8% for workers' compensation payers** due to an ongoing decline in utilization and lower overall cost per Rx

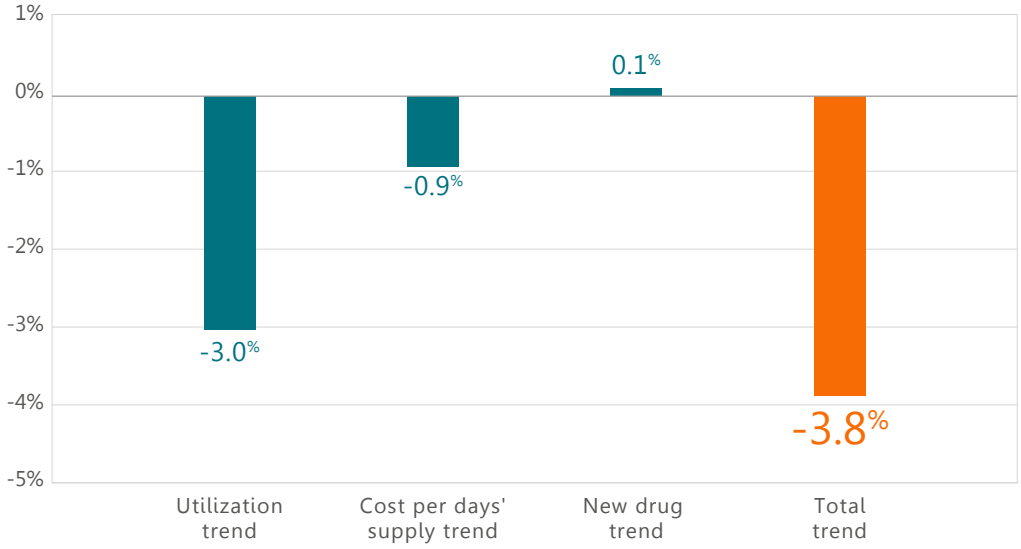
53.3%
of plans we managed reduced drug spending last year

15.0%
reduction in opioid spending due to:

- PBM clinical pharmacy solutions, including aggressive management of opioid prescribing
- Education programs for prescribers and claims professionals
- New state and federal regulations on opioid prescribing

WORKERS' COMPENSATION PLAN DRUG TREND

2018 (compared to 2017)



Turning the tide on opioid use

Average **spending on opioids declined 15.0% for our workers' compensation payers**, from $316.40 to $268.88 per patient per year

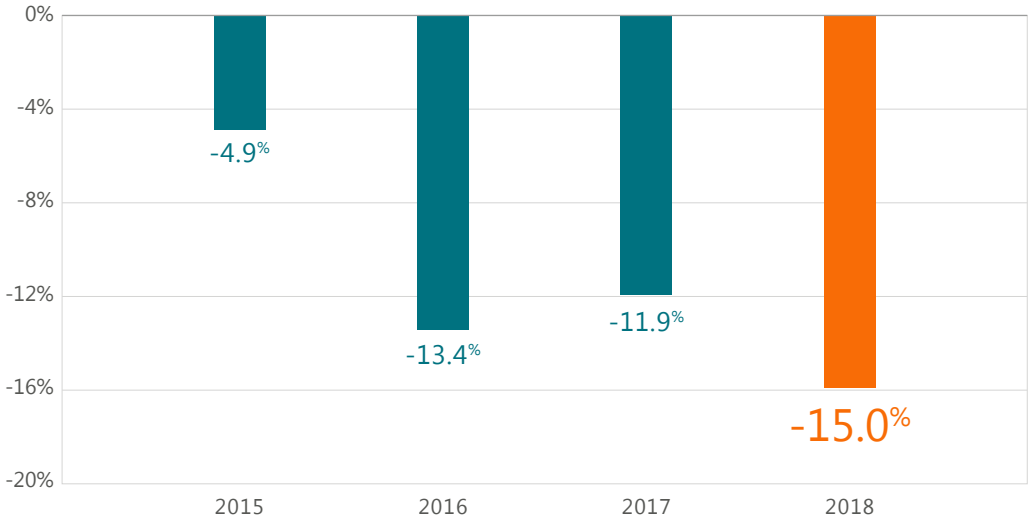
65.9%
of payers spent less on opioids in 2018 compared to 2017

17.6%
of injured workers used opioids for 30 or more days, down from 21.0% in 2017

$515.39
lower cost for generic, non-abuse deterrent formulation (ADF) vs. branded abuse-deterrent formulations (ADFs), per adjusted Rx

SPENDING ON OPIOIDS

2015-2018



↓ 40.4% since 2015

Thwarting dangerous combinations

Some injured patients were prescribed an opioid with a muscle relaxant, a benzodiazepine or both. Since the resulting combinations can be dangerous, their co-prescribing is discouraged by Official Disability Guidelines (ODG) and American College of Occupational and Environmental Medicine (ACEOM). Further, the misuse of Lyrica®/Lyrica® CR (pregabalin) or gabapentin in combination with opioids, which is on the rise, significantly increases the risk of opioid-related mortality. Gabapentin misuse has led to its scheduling as a controlled substance in several states and/or its reporting to prescription drug monitoring programs (PDMPs). Pregabalin already is a Schedule IV controlled substance at the federal level. Our holistic approach to opioid management resulted in reducing the use of many dangerous combinations, including opioids and benzodiazapines down from 5.3% in 2017 to 4.8% in 2018.

25.8%
used an opioid and a muscle relaxant

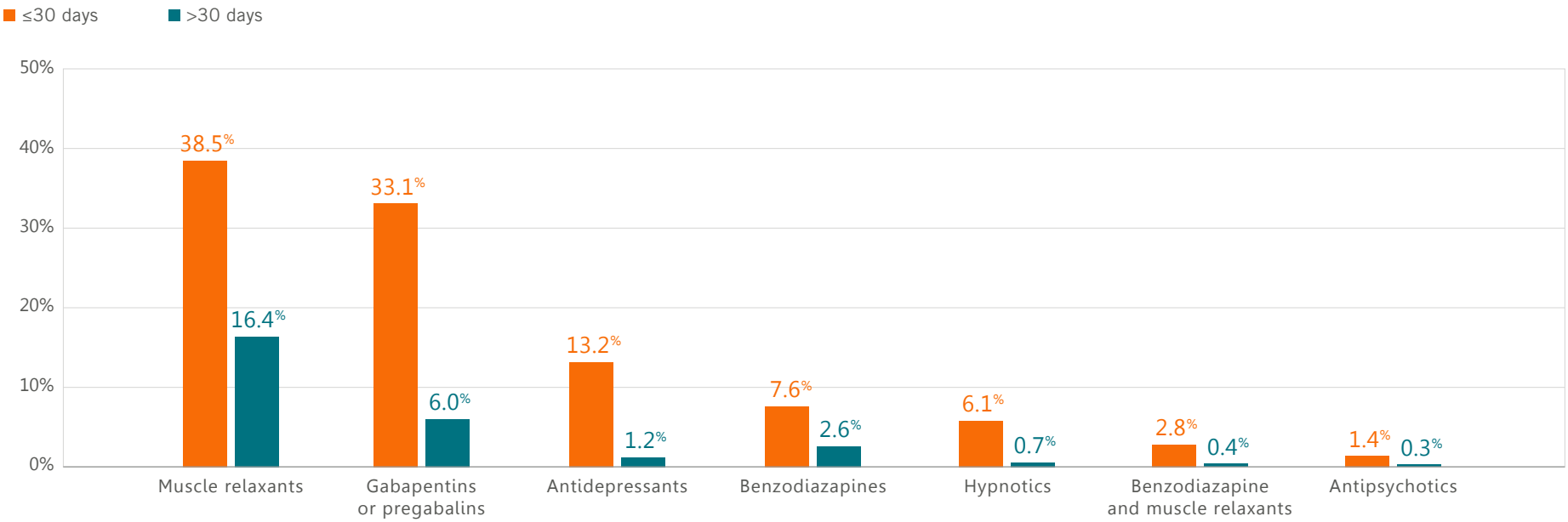
17.6%
used an opioid and gabapentin/pregabalin

4.8%
used an opioid and a benzodiazepine

1.4%
used an opioid, a muscle relaxant and a benzodiazepine

PERCENT OF INJURED WORKERS USING OPIOIDS IN POTENTIALLY DANGEROUS COMBINATIONS

By combination type and usage duration, 2018



Turning the tide on opioid use

Use of opioid overdose agent for opioid overdose by injured workers increased in 2018

In the fight against opioids, some states added naloxone and/or its branded counterparts, Narcan® and Evzio®, to their formularies per practice guideline recommendations. Thirty-three states and the District of Columbia now provide legal immunity for individuals who seek medical aid for a potential opioid overdose victim.[1] As of July 1, 2017, every state has at least one law that eases access to naloxone. As a result, opioid overdose deaths have decreased by 9% to 11%.[2] At myMatrixx, we consider naloxone use to be a factor when assessing drug-related risk for patients in our CARE analytics program. Monitoring naloxone use allows our clinical pharmacists to consult with prescribers regarding ways to lower the patient's overdose risk.

4 out of 1,000

(0.40%) injured workers filled an opioid overdose agent prescription in 2018 (up from 0.19% in 2017)

Age-of-injury effect: The longer an injured worker takes medication for an injury, the more costs rise.[3]

First year

$212.98
average cost per injured worker

$16.24
for opioids

>10 years

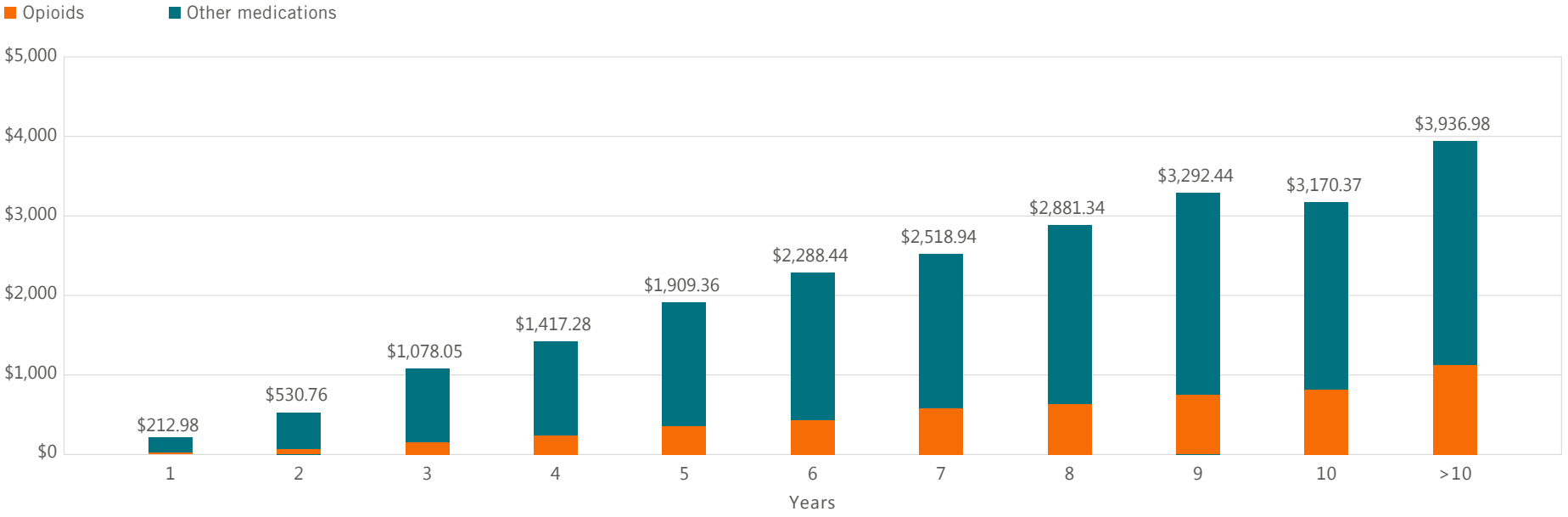
$3,936.98
average cost per injured worker

$978.68
for opioids

Click for table

TOTAL COST PER INJURED WORKER

By age of injury, 2018

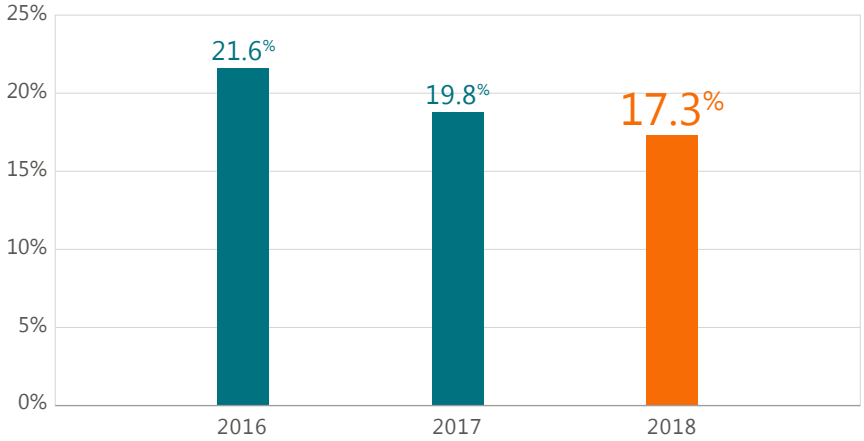


Utilization of other drugs for managing pain

As prescribers turn to non-opioid drugs for pain management, formulary controls and other aspects of our pharmacovigilance program are vital to ensure that the end result is more beneficial therapy. Our analysis indicates that non-steroidal anti-inflammatory drugs (NSAIDS) and gabapentin, preferred alternatives for pain management, are the only pain medications with an increase in utilization among our payers. Drugs of concern, such as benzodiazepines and sedative hypnotics, decreased in use, while use of other pain drugs showed no changes.

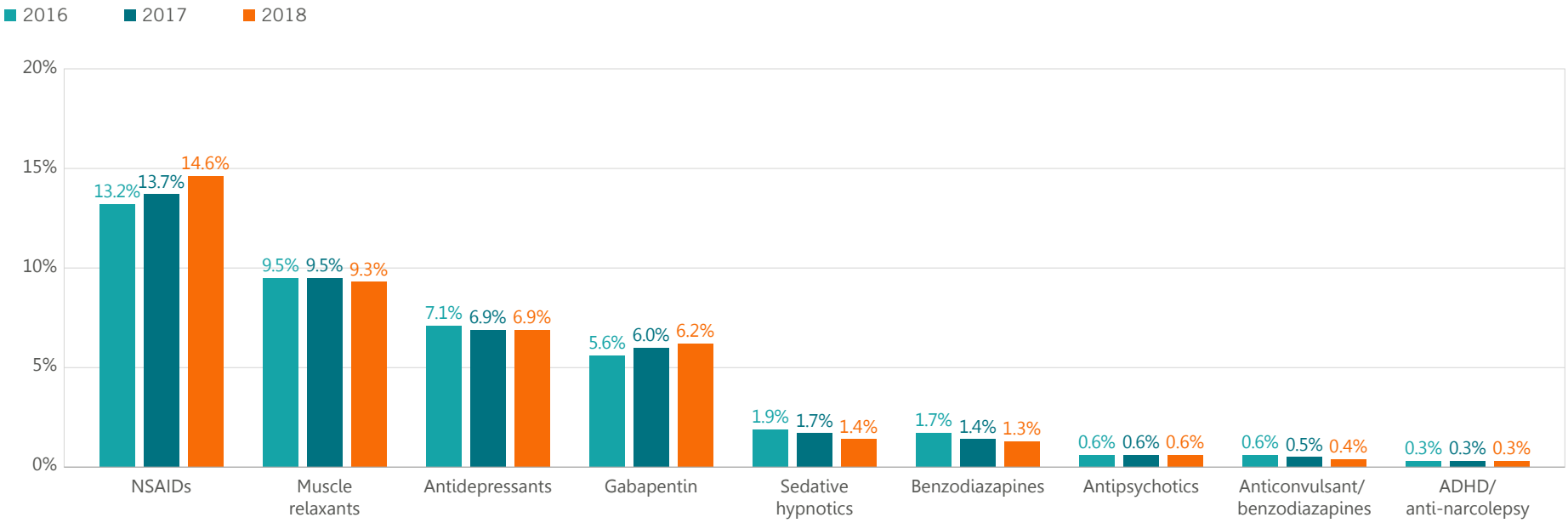
OPIOID USAGE

Percentage of total days' supply, 2016-2018

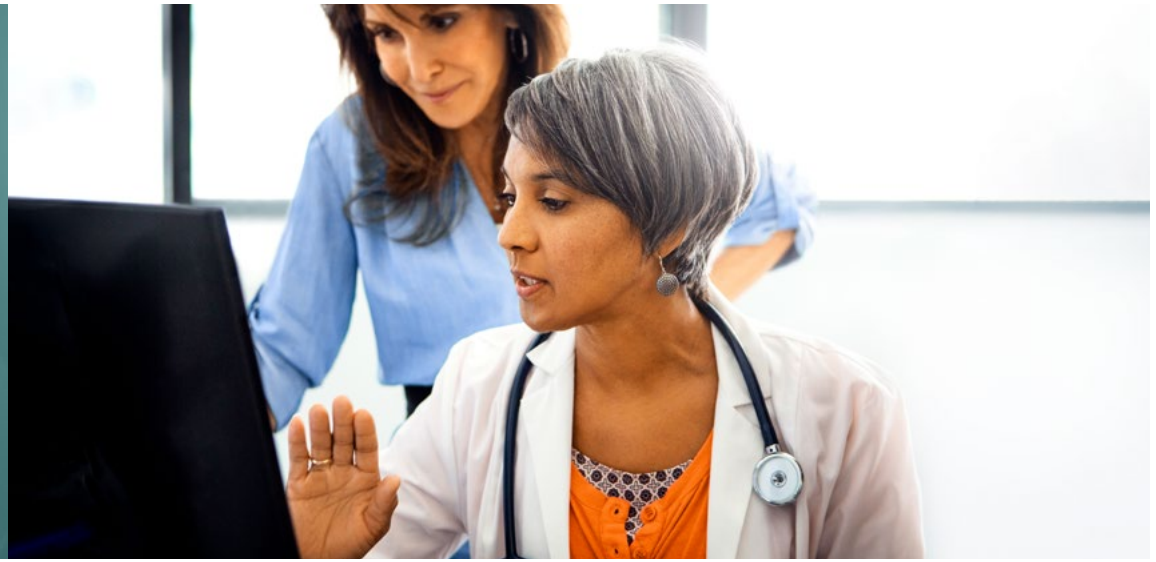


NON-OPIOID PAIN MEDICATION USAGE

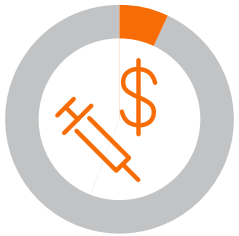
Percentage of total days' supply, by drug category and year, 2016-2018



Managing rising spend for specialty therapies



Specialty drug spending increased 18.5%
for workers' compensation payers in 2018



7.1%
specialty drug spend as a percentage of total workers' compensation drug spend, despite just 1.7% of injured workers using a specialty drug

7.2%
increase in specialty drug utilization, to 1.40 days' supply per patient per year in 2018

The disparity between utilization and spend – only 1.7% of claims driving 7.1% of spend – means that many workers' compensation payers may never encounter specialty drugs. However, for those payers who do have specialty claims, the financial impact is likely to be significant. Authorization decisions for drug therapy in workers' compensation are complex, and they may have a large impact on payer pharmaceutical spending. For example, one of the most expensive drugs identified on page 9 treats a rare condition deemed compensable for a single patient.

Worker populations most likely to receive a specialty drug include:
- Emergency first responders
- Public safety personnel
- Law enforcement officers
- Correctional officers
- Health care workers
- Certain defined workers in states with cancer presumption laws

Our previous report, Specialty Drugs in Workers' Compensation: A Population-Based Assessment, provides insights on the specialty drug market.[4]

Managing rising spend for specialty therapies

19.2%

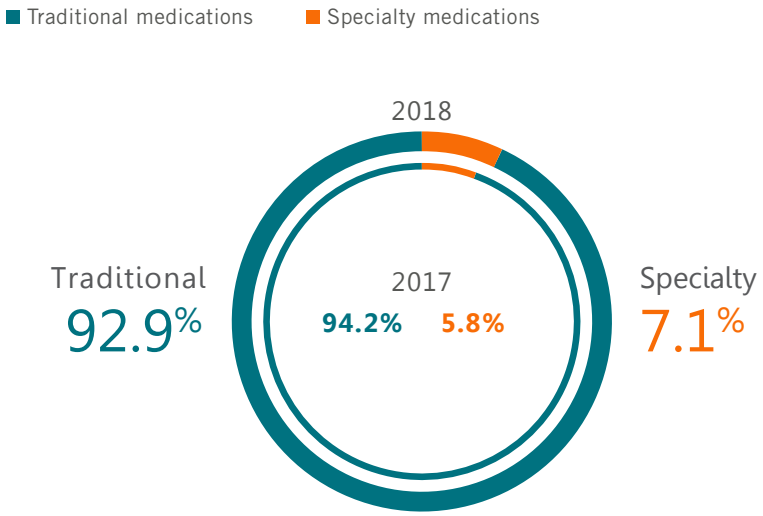
increased use of HIV medication in 2018 for post-exposure prophylaxis, as included in some payers' first-fill and acute formularies

Specialty drugs in the pipeline (or recently approved) that may influence workers' compensation specialty trend in the next few years:

- **Adalimumab** – biosimilars for Humira®
- **Esketamine intranasal** – a non-competitive NMDA receptor antagonist for treatment-resistant depression when used in combination with an oral antidepressant
- **Eptinezumab** – CGRP inhibitor for migraines, IV therapy
- **Upadacitinib** – JAK-1 inhibitor for moderate-to-severe rheumatoid arthritis

PERCENT OF SPEND

2017-2018



TOP 10 SPECIALTY THERAPY CLASSES

By per-patient-per-year spend, 2018

Click for top 10 medications

	COST		TREND		
CONDITIONS	PPPY SPEND	COST PER DAYS' SUPPLY	UTILIZATION	COST PER DAYS' SUPPLY	TOTAL
HIV	$21.38	$55.58	10.9%	7.5%	**19.2%**
Oncology	$9.23	$335.52	14.6%	1.0%	**15.7%**
Inflammatory conditions	$8.55	$177.71	11.0%	15.9%	**28.7%**
Osteoarthritis	$6.26	$36.41	-19.1%	-9.7%	**-26.9%**
Hereditary angioedema	$6.15	$5,950.31	1107.0%	-80.3%	**138.1%**
High blood cholesterol	$6.14	$40.82	82.1%	1.0%	**83.8%**
Pulmonary hypertension	$3.97	$110.06	14.7%	-7.4%	**6.2%**
Anticoagulant	$3.48	$39.10	-4.1%	0.5%	**-3.7%**
Asthma	$3.03	$135.66	17.6%	11.6%	**31.2%**
Transplant	$2.87	$11.35	-2.1%	-11.7%	**-13.5%**

Planning for higher costs for older workers

Costs escalate for injured workers in older age groups

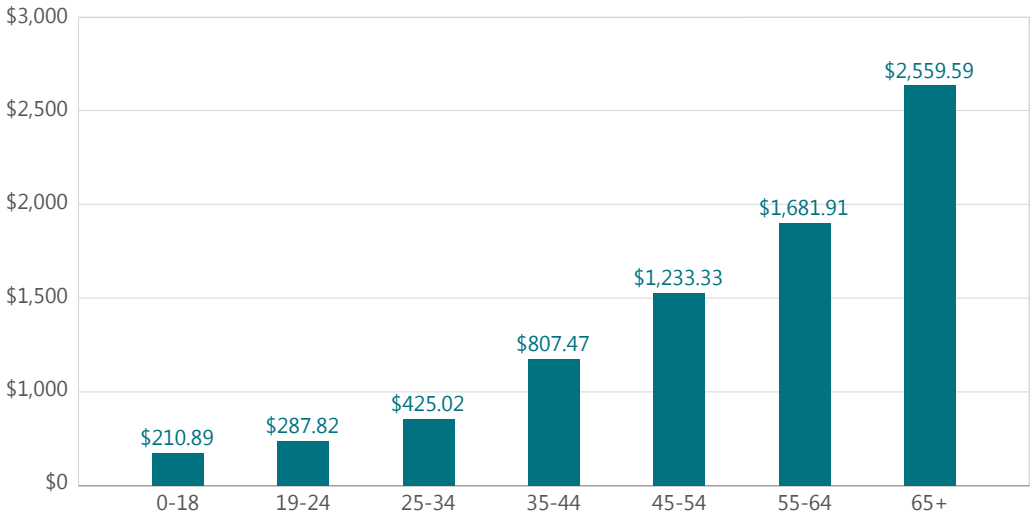
25%
of workforce will be 55+ years of age by 2024[5]

$1,959.55
higher costs per injured worker age 55+ (vs 0-55) in 2018

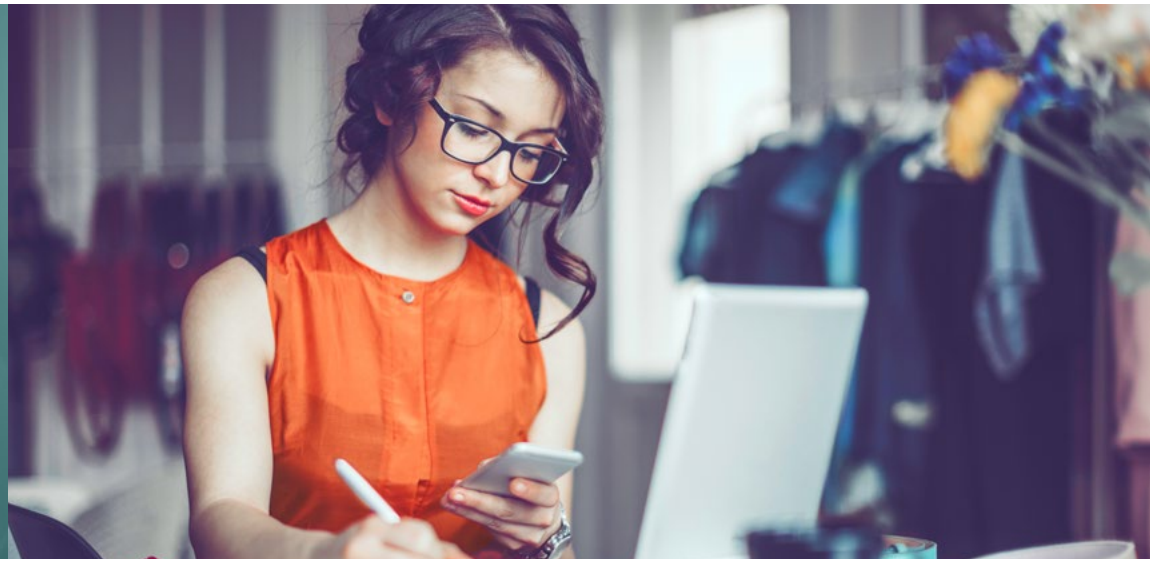
COST PER PATIENT

By age, 2018

Click for table



Controlling unit costs for workers' compensation plans

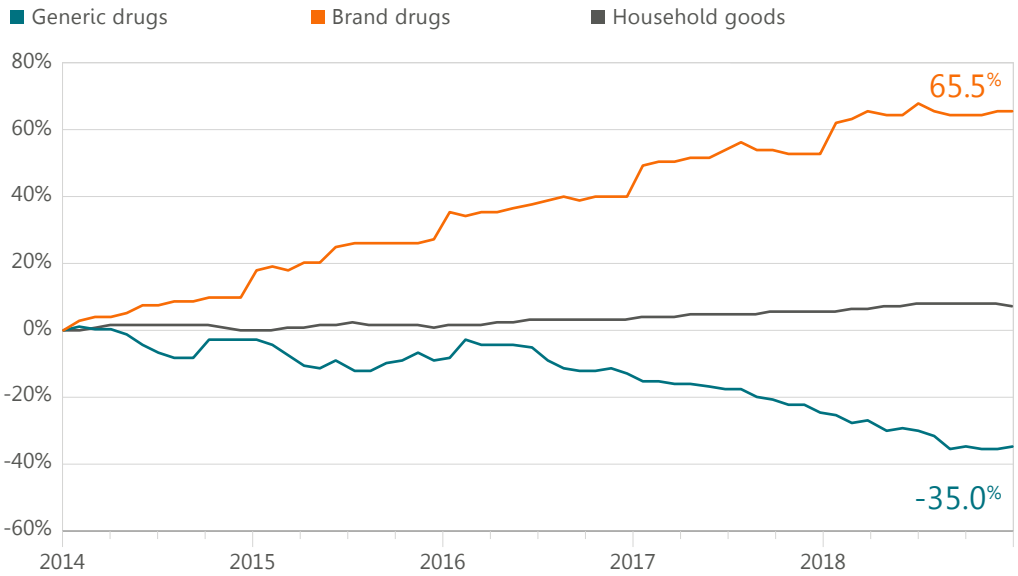


Unit cost per days' supply **decreased by 0.9% in 2018**

Over the past five years, the most commonly used brand-name traditional drugs among injured workers experienced list price inflation of 65.5%, but prices for the mostly commonly used generic medications declined 35.0%. In contrast, a market basket of commonly used goods (e.g., milk, bread, etc.) rose only 7.4%.

MYMATRIXX OVERALL PRESCRIPTION PRICE INDEX

2014-2018



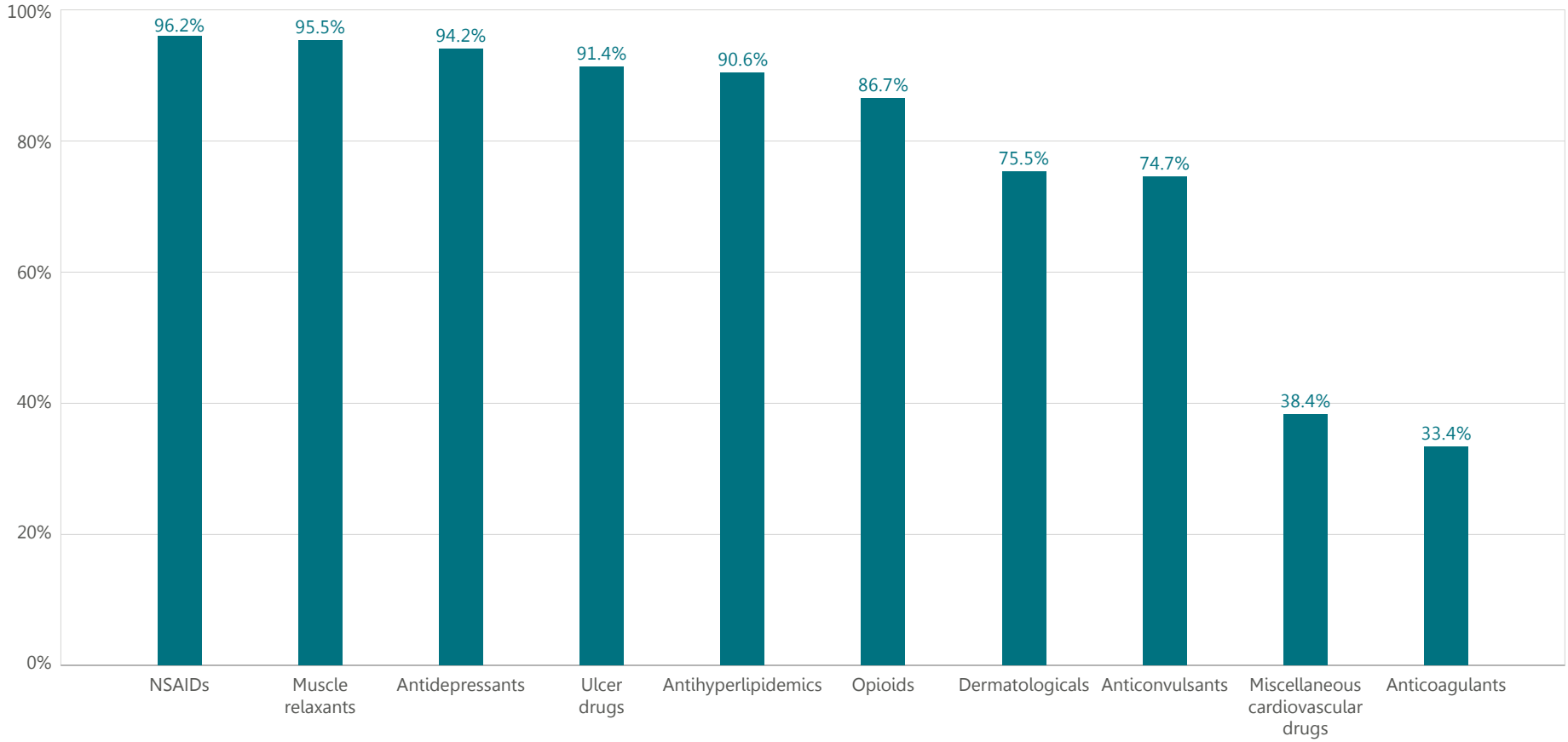
Enabling greater value by maximizing generic use

85.6%

generic fill rate (GFR) across all myMatrixx workers' compensation payers in 2018

GENERIC FILL RATE

By condition, 2018



Driving use of compounded medications to a new low

Spending on compounded medications **declined another 42.3% in 2018**

Typically, compounded medications are excluded from workers' compensation formularies, including state-specific formularies, and usually, they require review prior to dispensing for an injured patient.

4
years in a row that payer spending on compounded drugs has decreased

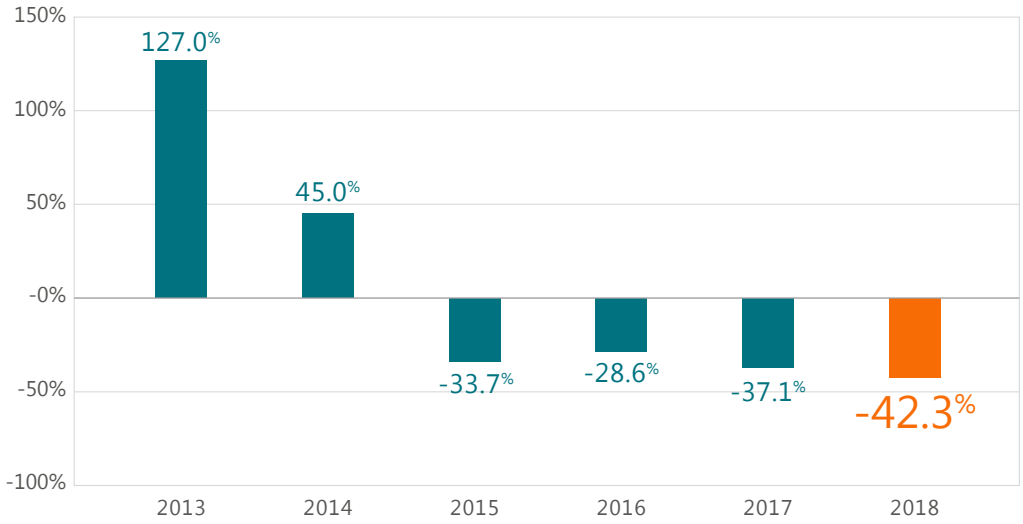
24.1%
decrease in utilization of compounded medications since 2017

0.2%
of prescriptions were for compounded medications

18.2%
reduction in average cost per days' supply

WORKERS' COMPENSATION COMPOUNDED DRUG TREND

2013-2018



Reducing waste through channel optimization

Waste occurs when drugs are dispensed through a costlier channel than necessary **with no incremental gain in health**

20.7%
lower cost for prescriptions filled through home delivery vs. retail pharmacies

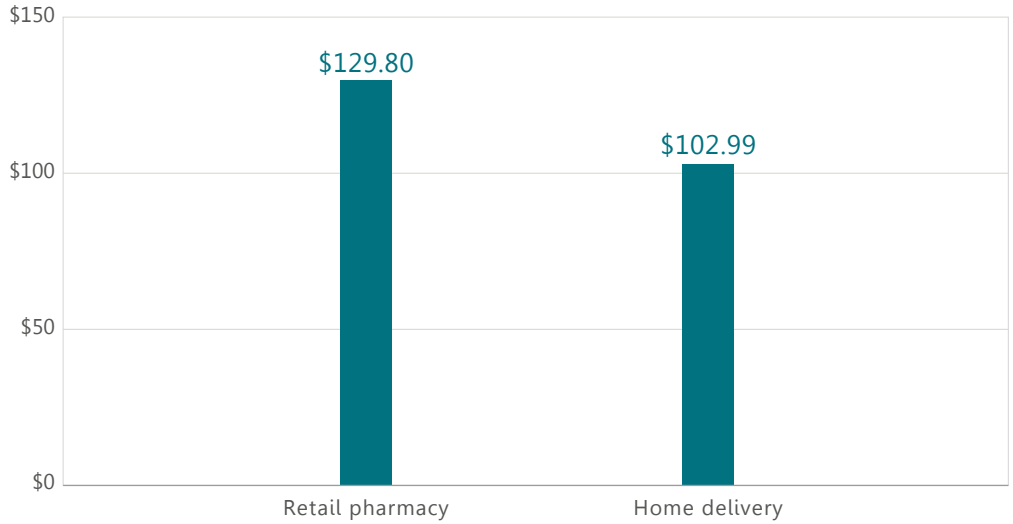
95.8%
of medications filled through home delivery are non-opioids

Injured workers use medications such as opioids or drugs to treat acute injuries that are not typically filled through home delivery. For workers with more catastrophic injuries or those taking medications for a chronic condition, home delivery can provide savings for payers and convenience for patients.

Click for more details

AVERAGE COST PER ADJUSTED Rx

Retail pharmacy vs. home delivery, 2018



Mapping out government regulations

The adoption of state-specific formularies was significant in 2018 – New regulatory language addressed various issues, including opioid dispensing, compound prior authorization (PA) and physician PA, within the workers' compensation industry

The following states adopted or will be implementing a state-specific formulary:

- **California** (effective 1/1/18)
- **Arkansas** (effective 7/1/18)
- **Indiana** (effective 1/1/19)
- **Montana** (effective 4/1/19)
- **Kentucky** (effective 7/1/2019)

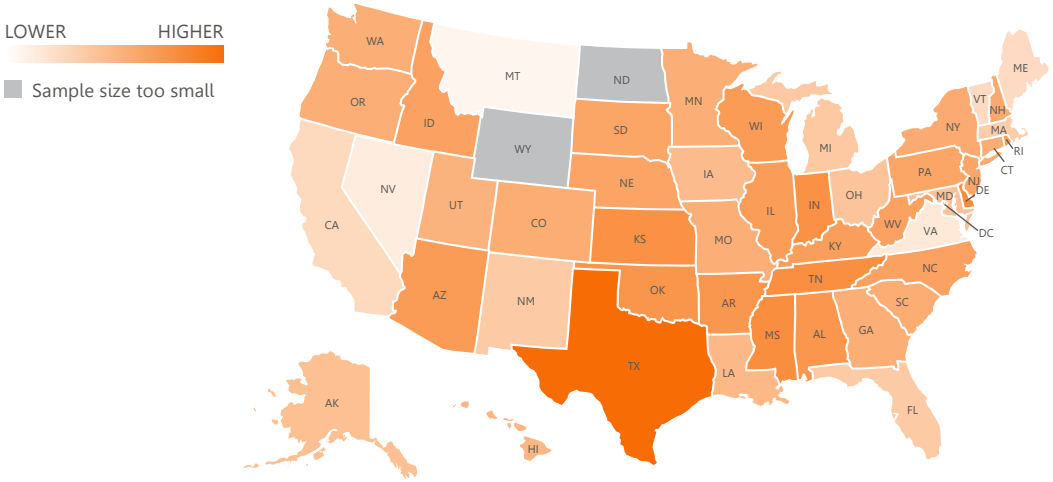
A few states, including California and Kentucky, adopted prior authorization and limitation requirements for physician dispensing.

Many states have also taken a step forward in adopting opioid-related controls, including prescribing and dispensing limitations. Arizona, Colorado, Florida, Hawaii, Michigan, Minnesota, North Carolina, Oklahoma, Pennsylvania, South Carolina, Texas and West Virginia are among the states to adopt opioid rules, regulations and/or guidelines in 2018.

Click for table

PERCENT OF PRESCRIPTIONS ON FORMULARY

By state, 2018



This map provides a snapshot of the steps taken by states to address pharmacy-related challenges in workers' compensation, specifically formulary.

Top 10 therapy classes and insights

The top 10 therapy classes accounted for 78.5% of total workers' compensation drug spending in 2018

$1,211.53

average amount spent by payers per injured worker for prescription medications in 2018

21.7%

higher costs per days' supply for anticoagulants

19.5%

rise for dermatologicals in PPPY spend

Both were offset by low and negative average costs per prescription in most classes for an overall moderating impact on trend.

Five of the top 10 therapy classes in 2018 had utilization decreases, including significant declines in the use of opioids, and less use of muscle relaxants, anticonvulsants, antidepressants and ulcer drugs. New to the top 10 for 2018, the anticoagulant class (blood thinners) was driven primarily by a 21.7% increase in average cost per days' supply. These medications may be used post-surgery or may be covered by some payers depending on their injured worker population. It is important to note that this increase in cost is driven by Eliquis® (apixaban) and Xarelto® (rivaroxaban), which are both specialty drugs; while spend for the traditional anticoagulant, warfarin, actually is decreasing.

Click for components of trend

TREND FOR THE TOP 10 THERAPY CLASSES

By per-patient-per-year spend, 2018

THERAPY CLASS	TOTAL TREND
Opioids	-15.0%
Anticonvulsants	1.1%
Dermatologicals	19.5%
NSAIDs	-3.9%
Antidepressants	-9.5%
Muscle relaxants	-2.5%
Ulcer drugs	-7.8%
Antiasthmatics	4.5%
Anticoagulants	28.0%
Miscellaneous cardiovascular drugs	-0.6%
Total	**-3.8%**

Looking forward: What's on the horizon for 2019 and beyond?

PIPELINE DRUGS TO WATCH

2019-2020

DRUG NAME	MOST COMMON INDICATION	EXPECTED FDA APPROVAL
buprenorphine/samidorphan	Depression	2019
bupivacaine/meloxicam	Pain and inflammation	2019
lasmiditan	Migraine headache	2019
rimegepant	Migraine headache	2020
ubrogepant	Migraine headache	2020

Looking forward: What's on the horizon for 2019 and beyond?

TOP DRUGS LOSING PATENT PROTECTION

2019-2022

DRUG NAME	MOST COMMON INDICATION	SCHEDULED YEAR
Advair Diskus® (fluticasone/salmeterol)	Asthma	2019
Amitiza® (lubiprostone)	GI disorders	2021
Amrix® (cyclobenzaprine)	Muscle relaxant	2019
Dexilant® (dexlansoprazole)	Heartburn/ulcer disease	2020-2023
Fentora® (fentanyl buccal tablets)	Pain/inflammation	2019
Fetzima® (levomilnacipran)	Depression	2019
Flector® (diclofenac epolamine patch)	Pain/inflammation	2019
Flovent® HFA (albuterol)	Asthma	2019-2020
Forteo® (teriparitide)	Osteoporosis	Q3/Q4 2019
Jublia® (efinaconazole)	Skin infections	2021
Lyrica® CR (pregabalin)	Pain/inflammation	2021-2022
Lyrica®/Lyrica® oral solution (pregabalin)	Pain/inflammation	2019
Oxaydo® (oxycodone)	Pain/inflammation	2022
Perforomist® (formoterol)	Asthma	2021
ProAir® HFA (albuterol)	Asthma	2019-2020
Proventil® HFA (albuterol)	Asthma	2019-2020
Relistor® (methylnaltrexone)	Constipation	2019
Rozerem® (ramelton)	Sleep disorders	2019
Silenor® (doxepin)	Sleep disorders	2020
Sprix® (ketorolac)	Miscellaneous conditions	2019
Suboxone® sublingual film (buprenorphine/naloxone)	Addiction	2019
Viibryd® (vilazodone)	Depression	2020-2021
Vimovo® (naproxen/esomeprazole magnesium)	Pain/inflammation	2022
Vimpat® (lacosamide)	Seizures	2022
Vivlodex® (meloxicam)	Pain/inflammation	2019
Zipsor® (diclofenac)	Pain/inflammation	2022
Zohydro® ER (hydrocodone)	Pain/inflammation	Q4 2019
Zomig® Nasal (zolmitriptan nasal spray)	Migraine headache	2021

While some of these drugs are not typically used in workers' compensation programs, payers with certain patient populations may deem them related to an occupational injury.

Exploring future pharmacy-related trends

Precision medicine delivers individualized therapy regimens

Pharmacogenetics typically relates to the effect of deviation in one gene on one drug. Pharmacogenomics is more inclusive. It takes into account how the individual's whole genome (the set of genes and genetic variations unique to that person) could affect drug effectiveness.[6] With the completion of the Human Genome project in 2003, scientists often can determine how inherited differences in genes may affect the body's response to medications. These genetic differences can be used to predict whether a medication will be effective or have adverse drug reactions for an individual.

Additionally, an individual's unique genetic makeup may cause differences in the way the body metabolizes (breaks down) drugs to facilitate their removal from the body once inactive. Metabolites, the substances from drug metabolism, may be active or inactive. An active metabolite can be much different from the drug in its therapeutic activity, toxicity or both.[7] Metabolizing a drug more quickly than expected may result in a poor response, risking pharmacotherapy failure. Slower than usual metabolism could result in higher blood levels of the drug, which may lead to adverse drug reactions. Knowing ahead of time how an individual metabolizes certain drugs helps to plan appropriate pharmacotherapy. This approach of tailoring medicine to an individual patient is known as precision, personalized or individualized medicine.

Genetic differences can be used to predict whether a medication will be effective or have adverse drug reactions for an individual

What does this mean for workers' compensation?

Payers may be starting to see charges associated with precision medicine. For example, genetic testing may be recommended for their injured workers. While costly, these tests can improve patient outcomes and save payers money in the end if they are used appropriately.

Drug classes in which genetic testing may play a role include:

- **Anticoagulants** (apixaban, dabigatran, rivaroxaban, warfarin)
- **Platelet inhibitors** (clopidogrel)
- **Proton pump inhibitors** (esomeprazole, lansoprazole, pantoprazole)
- **Opioids** (codeine, tramadol, oxycodone, hydrocodone)
- **SSRI antidepressants** (escitalopram, fluoxetine, paroxetine, sertraline)

Personalized medicine will continue to evolve as technologies improve and barriers to clinical implementation, such as clinical education, expanded expertise, regulation, guidelines and recommendations, costs and reimbursement, are overcome.[8] myMatrixx will continue to monitor the expansion of personalized medicine and establish programs to best meet the changing needs of our clients.

New HIV therapies may enable greater adherence

The HIV pipeline includes new long-acting injectable drugs – a monoclonal antibody and a combination. Because adherence to therapy is often a barrier to positive outcomes in patients living with HIV, the convenience of drugs that do not have to be taken orally and daily may help those living with HIV to keep the infection under control.

Leronlimab (PRO 140) is a monoclonal antibody/CCR5 chemokine receptor antagonist in a new class of HIV/AIDS therapies known as viral-entry inhibitors. CCR5, a protein on the surface of some immune system cells, is used by HIV to enter host cells. Masking the precise sites on CCR5 that HIV needs protects healthy cells from becoming infected. It is a once-weekly, subcutaneous (SC) injection. Currently in Phase 3 clinical trials, its approval from the U.S. Food and Drug Administration (FDA) is anticipated in 2020.[9]

Drugs that do not have to be taken orally and daily may help those living with HIV

Cabotegravir/rilpivirine is an injectable integrase strand transfer inhibitor/non-nucleoside reverse transcriptase inhibitor (NNRTI) combination. Cabotegravir is a new member of the drug class that blocks activity of integrase, an enzyme that HIV needs to multiply.

Phase 2 clinical trials of its use found that when administered intramuscularly, cabotegravir has a mean half-life of between 21 and 50 days (the time it takes for the concentration of a drug in the plasma or the total amount in the body to be reduced by 50%).[10]

Under the brand-name, Edurant®, rilpivirine currently is being used as oral HIV therapy.[11] Its long-acting intramuscular suspension form is not yet approved. The combination of the two drugs, administered intramuscularly once a month, currently is in Phase 3 clinical trials with possible FDA approval in 2020.

Anticipating the possibility of an addiction-free opioid

According to a 2018 study published in the medical journal Science Translational Medicine, scientists at Wake Forest School of Medicine in North Carolina have discovered a compound, AT-121, that provides opioid-level pain relief without causing addiction or overdose for laboratory animals.[12]

Like currently available opioids, AT-121 targets mu opioid receptors, but it also activates another group of receptors known as nociceptin/orphanin FQ peptide (NOP) receptors. Although activation of mu opioid receptors located throughout the brain and spinal cord leads to pain relief, it also causes other reactions, such as euphoria and respiratory depression (i.e., the mechanisms leading to addiction, overdose and death). Activation of the NOP receptors counteracts the adverse reactions while maintaining pain relief. Researchers who tested AT-121 on rhesus monkeys, found that it is 100 times more potent than morphine for pain relief.

It does not, however, induce opioid side effects such as respiratory depression, opioid-induced hyperalgesia (abnormal sensitivity to pain) and physical dependence. Its potential for abuse and physical dependence appears to be low.

AT-121 is 100 times more potent than morphine for pain relief

The next step in development is human studies. If the effects of AT-121 are as positive in humans as in monkeys, it has great potential to offer a safer alternative for management of intense, chronic pain. Given the lengthy path to FDA approval, though, AT-121 will take many years to become available to patients.

In the meantime, standard opioids will remain the conventional choice for severe pain and they will continue to plague patients with a myriad of side effects up to and including death.

Methodology

In calculating trend, prescription drug use was considered for clients with a stable injured-worker base, defined as having a change in patient volume of less than 50% from 2017 to 2018.

Nonprescription medications and prescriptions that were dispensed in hospitals, long-term care facilities and other institutional settings were not included in our analysis.

Utilization, determined on a per-patient-per-year (PPPY) basis, was calculated by dividing the total days' supply of medications by the total number of patients in a year.

Market share was determined by calculating the percentage of total days' supply of medication represented by each medication in a therapy class.

Prescription drug costs were calculated by adding together ingredient cost, taxes, administrative fees and dispensing fees.

All images are for representative purposes only and do not depict actual patients or prescribers.

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