California Workers' Compensation Institute

Spotlight Report

Cost-Driver Medications in the Top California Workers' Comp Therapeutic Drug Groups, Part 3: Musculoskeletal & Ulcer Drugs

Bob Young and Stacy L. Jones **July 2023**

Background

According to CWCI's Prescription Drug Application,[1] seven therapeutic drug groups accounted for at least 5 percent of all California workers' compensation prescriptions in 2021: Anti-Inflammatories; Anticonvulsants; Dermatologicals; Opioids; Antidepressants; Musculoskeletals; and Ulcer Drugs. Combined, these seven groups represented 82.3 percent of the prescriptions filled in 2021, and 69.2 percent of the total drug spend.

A review of the specific drugs within each of the seven drug groups revealed that often, the most heavily prescribed medications are relatively inexpensive, so even though they represent a large share of the prescriptions, they consume a disproportionately low percentage of the total payments. On the other hand, within each of these drug groups the Institute identified a handful of high-priced medications – some of which were not well-known – that account for a relatively small share of the prescriptions, but due to their high average reimbursements, have become significant cost drivers within their groups.

In early 2023, CWCI initiated a 3-part research series to raise awareness of these low-volume/high-cost drugs and the factors that underlie their high average reimbursements. Part I of the series, published in March, focused on Anti-Inflammatories and Anticonvulsants,[2] which now rank first and second in terms of California workers' compensation prescription volume; while Part II, published in May, focused on Opioids, Dermatological Drugs, and Antidepressants,[3] which rank third, fourth, and fifth respectively. This report completes the series by taking an in-depth look at the final two of the top seven therapeutic drug categories: Musculoskeletal and Ulcer Drugs. The report highlights three types of musculoskeletal prescriptions: viscosupplements, which are physician-administered preparations (rather than dispensed medications) containing hyaluronic acid that are injected into knees or other joints; chlorzoxazone caplets, used to treat muscle spasms and musculoskeletal pain; and metaxalone tablets, which is used as a muscle relaxant and to relieve pain caused by strains, sprains, and other musculoskeletal conditions. The report also examines three Ulcer Drugs which are proton pump inhibitors that reduce the amount of acid produced in the stomach: lansoprazole; esomeprazole magnesium; and dexlansoprazole.

---

[1] CWCI's Prescription Drug Application is an online tool available to CWCI members at www.cwci.org.

[2] Young, B., Jones, S. *Cost-Driver Medications in the Top California Workers' Comp Therapeutic Drug Groups, Part I: Anti-Inflammatories and Anticonvulsants*, CWCI Spotlight Report, March 2023.

[3] Young, B., Jones, S. *Cost-Driver Medications in the Top California Workers' Comp Therapeutic Drug Groups, Part II: Dermatologicals, Opioids, and Antidepressants*, CWCI Spotlight Report, May 2023.

Data and Methods

CWCI's Prescription Drug Application contains detailed data on California workers' compensation prescriptions compiled from the Institute's Industry Research Information System (IRIS) database.[4] Each drug within the application is identified by its National Drug Code (NDC) and descriptive information from Medi-Span,[5] including the therapeutic drug group, active ingredient name, and its availability as a brand name or generic drug. The January 3, 2023 version of the application contains data on nearly 9.5 million prescriptions dispensed to injured workers between January 2010 and June 2022, with aggregate payments for those prescriptions totaling nearly $1.02 billion.

The service year detail in the application ranks the top drug groups based on prescription volume, and for this research series the authors limited the sample to drug groups that accounted for at least 5 percent of service year 2021 prescriptions. Including the Anti-Inflammatories and Anticonvulsant Groups that are the focus of this initial analyses, there were seven therapeutic drug groups that accounted for at least 5 percent of all California workers' compensation prescriptions in 2021 (no other drug groups represented more than 2.1 percent of the prescriptions).

For the research series, the authors used service year 2021 data from CWCI's Prescription Data Application to rank the individual drugs within the top seven drug groups based on their percentage of the dispensed medications and total payments within the group. The application includes preliminary data on prescriptions dispensed through June 2022, but the service year 2022 prescription data was not sufficiently developed for comparisons to full-year data from prior years, so the 10-year trends for the drug groups and individual drugs detailed in this research series are based on service year 2012 through service year 2021 prescription data, reported as of June 30, 2022.

In addition, because the prescription drug market is constantly evolving as new medications are introduced, older medications are retired or reformulated, patents on brand drugs expire and generic versions hit the market, and revisions are made to the Medical Treatment Utilization Schedule (MTUS) Prescription Drug Formulary, the authors focused on medications dispensed in service year 2021 (the most recent full-year data included in the Prescription Data Application) to identify those drugs that are consuming a disproportionately high share of the total dollars paid within the drug group relative to their share of the prescriptions.

The authors also used the service year detail to note changes in the average amount paid per prescription for each drug within the 10-year study period, as well as the percentage that were dispensed as brand drugs rather than as generics. Additional detail from the IRIS database identified where the medications was dispensed, the form in which they were dispensed, specific brands that were used, and additional pricing information.

[4] IRIS is CWCI's proprietary transactional database of insured and self-insured policies and their associated claims. Version 2022Q2, used for the latest version of the Prescription Drug Application contains detailed data on employee and employer characteristics, medical service data, benefits, and administrative costs on more than 7.6 million California workers' compensation claims.

[5] Master Drug Data Base (MDDB) Version 2.5 Documentation Manual, Wolters Kluwer Health, Medi-Span.

Objective

The goal of this research series is to identify relatively low-volume but high-cost medications within the top therapeutic drug groups currently used in California workers' compensation, (*i.e.*, those that consume a much higher share of the payments within their drug group relative to their share of the dispensed prescriptions within that group), and to determine the factors that are driving up the cost of these drugs and the extent to which those factors may be better controlled.

Findings

As noted in Exhibit 1, the top seven drug groups accounted for 82.3 percent of all California workers' compensation prescriptions filled in 2021, and that percentage showed only minor fluctuations over the 10-year span of the study, ranging from 81.1 percent to 83.6 percent. Opioids' share of the prescriptions registered the biggest drop, falling from 29.4 percent in 2012 to 9.4 percent in 2021, though the two drug categories highlighted in this report, Musculoskeletal and Ulcer drugs, also accounted for a declining share of the workers' compensation prescriptions, as Musculoskeletals fell from 9.7 percent to 5.9 percent of the prescriptions over that same decade, and Ulcer drugs fell from 7.1 percent to 5.4 percent.

In contrast to those declines, Anti-Inflammatories' share of the workers' compensation prescriptions nearly doubled from 17.7 percent to 34.8 percent over the 10-year study period, while Anticonvulsants jumped from 5.5 percent to 9.6 percent and Dermatologicals increased from 5.8 percent to 9.3 percent. Antidepressants' share of the prescriptions also rose, climbing from 5.9 percent in 2012 to 7.9 percent in 2021, with much of that increase (1.3 percentage points) occurring in the pandemic years of 2020 and 2021.

Exhibit 1: Top California WC Drug Groups* % of Prescriptions, 2012-2021

Therapeutic Drug Group	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	10-Yr %-age Point Change
Anti-Inflammatory	17.7%	18.2%	20.9%	24.1%	26.2%	27.4%	30.8%	33.6%	33.6%	34.8%	+17.1
Anticonvulsant	5.5%	5.8%	6.2%	6.9%	7.7%	8.5%	9.7%	10.0%	10.6%	9.6%	+4.1
Opioid	29.4%	28.7%	27.2%	23.9%	22.1%	19.6%	14.6%	11.3%	10.2%	9.4%	-20.0
Dermatological	5.8%	6.0%	5.8%	4.8%	5.0%	5.5%	6.4%	7.8%	8.5%	9.3%	+3.5
Antidepressant	5.9%	5.9%	5.3%	5.4%	5.5%	5.7%	6.4%	6.6%	7.1%	7.9%	+2.0
Musculoskeletal	9.7%	9.8%	10.1%	10.4%	10.6%	10.5%	7.0%	6.5%	6.4%	5.9%	-3.8
Ulcer	7.1%	7.3%	7.3%	7.1%	6.6%	6.4%	6.3%	6.1%	6.0%	5.4%	-1.7
Top 7 Subtotal	**81.1%**	**81.7%**	**82.8%**	**82.6%**	**83.7%**	**83.6%**	**81.2%**	**81.9%**	**82.4%**	**82.3%**	**+1.2**

* Drug group rankings based on 2021 prescription volume

The decline in Opioid utilization and the increase in the use of Anti-Inflammatories and other drugs that are often prescribed for off-label use as non-opioid analgesics led to a significant shift in the distribution of workers' compensation pharmaceutical payments over the 10-year study period. (Exhibit 2).

Exhibit 2: Top California WC Drug Groups* % of Total Drug Spend, 2012-2021

Therapeutic Drug Group	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	10-Yr %-age Point Change
Anti-Inflammatory	13.3%	13.1%	15.7%	17.6%	16.9%	14.6%	13.1%	15.5%	23.1%	24.5%	+11.2
Anticonvulsant	5.0%	5.4%	6.0%	7.1%	9.3%	11.4%	14.4%	14.0%	10.5%	8.1%	+3.1
Opioid	26.7%	24.8%	23.3%	20.7%	18.3%	16.0%	12.3%	9.4%	6.6%	5.8%	-20.9
Dermatological	12.8%	13.9%	13.4%	12.7%	16.1%	18.3%	16.3%	17.7%	15.2%	17.3%	+4.5
Antidepressant	5.9%	6.3%	4.8%	4.9%	4.4%	3.5%	3.4%	2.8%	3.2%	3.3%	-2.6
Musculoskeletal	5.6%	6.7%	5.8%	6.3%	6.7%	6.7%	4.1%	3.3%	4.6%	3.7%	-1.9
Ulcer	10.0%	9.7%	9.1%	8.9%	6.4%	6.8%	5.6%	5.9%	6.5%	6.5%	-3.5
Top 7 Subtotal	**79.3%**	**79.9%**	**78.1%**	**78.2%**	**78.1%**	**77.3%**	**69.2%**	**68.6%**	**69.7%**	**69.2%**	**-10.1**

* Drug group rankings based on 2021 prescription volume

While payments for Opioids declined from 26.7 percent of the total workers' compensation drug spend in 2012 to just 5.8 percent in 2021, Anti-Inflammatories' share of the payments climbed from 13.3 percent to 24.5 percent, Dermatological Drugs increased from 12.8 percent to 17.3 percent, and Anticonvulsants jumped from 5.0 percent to 8.1 percent, though the Anticonvulsant's share of the payments has declined since 2019, coinciding with the approval and introduction of generic pregabalin into the market. Pregabalin was the second most heavily prescribed Anticonvulsant throughout the 10-year study period, but prior to 2019, it was only available as a brand name drug (Lyrica). Drug categories that saw their share of the total drug spend decline over the decade included Ulcer Drugs (which are often prescribed for stomach issues that arise from the use of Opioids and Anti-Inflammatories) which dropped from 10.0 percent to 6.5 percent of the pharmaceutical dollars, Antidepressants, which fell from 5.9 percent to 3.3 percent of the prescription payments, and Musculoskeletal Drugs, which declined from 5.6 percent to 3.7 percent.

A number of market forces helped contribute to the changes in the mix of workers' compensation prescriptions and payments between 2012 and 2021, as new medications, formulations, and products were introduced (including extended release and tamper resistant versions of various drugs), patents on brand drugs expired and generic versions became available, and older medications were taken off the market. After reviewing the prescription drug utilization and payment data for medications within the top seven drug groups, the authors identified several relatively low-volume, high-priced medications that had a disproportionate impact on the costs within their drug group in 2021.

The following sections highlight the findings for what are now the sixth and seventh most heavily utilized drug groups, Musculoskeletals and Ulcer Drugs. Within these two groups the authors note the most significant "cost-driver" medications that were identified, each drug's share of the prescriptions within the drug category during service year 2021, the average amount paid per prescription, the percentage of the drug spend that the medication represented within the drug group, and the percentage of the drug that was dispensed as a brand-name drug rather than as a generic.

Musculoskeletals

Musculoskeletal Drugs are used to treat pain and stiffness in muscles and are commonly used to treat injured workers suffering from sprains, strains, or other injuries to muscles, some of the most common occupational injuries. From 2012 through 2017 the Musculoskeletal drug group represented between 9.7 and 10.6 percent of all California workers' compensation prescriptions, but because the most commonly dispensed drugs within the group are relatively inexpensive, Musculoskeletal prescriptions consumed between 5.6 and 6.7 percent of the total drug spend within the system. In 2018, following the adoption of the formulary which classified many of the Musculoskeletal Drugs as Non-Exempt drugs, requiring prospective utilization review, they declined to 7.0 percent of the prescriptions and 4.1 percent of the total payments, and by 2021 they were down to 5.9 percent of the prescriptions and 3.7 percent of the payments.

By far the most common Musculoskeletal Drug used in workers' compensation is the muscle relaxant cyclobenzaprine (*e.g.*, Flexeril); which since 2015 has accounted for more than half of the prescriptions in this drug group, and in 2021 ranked seventh among all workers' compensation drugs. Although the formulary categorizes cyclobenzaprine as a Non-Exempt drug, it is also listed as a Special Fill drug, so physicians may prescribe a four-day supply at an injured worker's initial visit that occurs within seven days of the injury without going through UR.

In addition to cyclobenzaprine, four other relatively low-cost medications have dominated the Musculoskeletal drug group: tizanidine HCl (*e.g.,* Zanaflex), which is also a Special Fill drug; baclofen (*e.g.*, Gablofen, Lioresal) which is both a Special Fill drug and a Perioperative drug, a limited supply of which can be prescribed during the four days prior to or after a surgery without going through UR; methocarbamol (*e.g.,* Robaxin), and carisoprodol (*e.g.*, Soma). Since 2012 nearly all of the workers' compensation prescriptions for these medications have been for generics, which has helped contain their cost. In 2021, cyclobenzaprine and these other four drugs together accounted for 90.7 percent of the Musculoskeletal prescriptions used to treat injured workers, but with average payments ranging from $14 to $40, they consumed just 27.5 percent of the overall musculoskeletal drug spend.

In contrast to the low-cost/ high-volume Musculoskeletal Drugs are three other medications that comprise only a small share of the Musculoskeletal prescriptions, but a disproportionately high percentage of the costs:

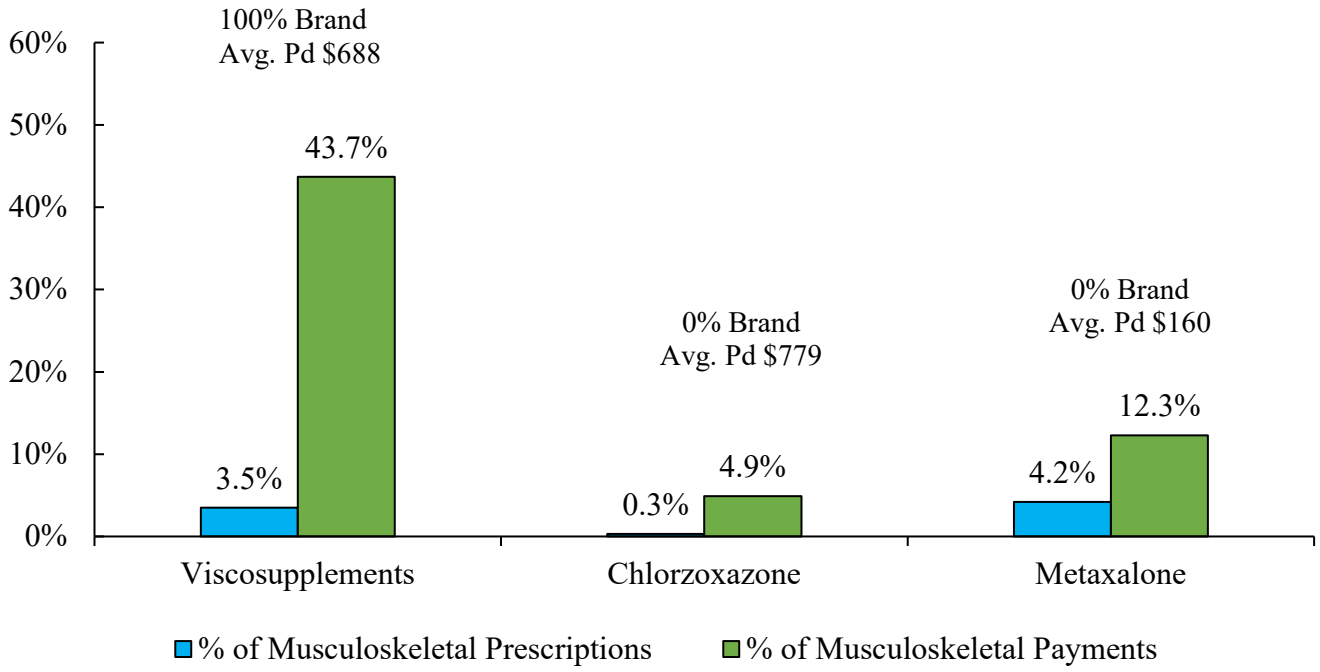
- Viscosupplements (*e.g.,* Hylan, Hyaluronan, and Sodium Hyaluronate) which are typically pre-filled syringes filled with gel-like agents that are injected into knees and other joints to lubricate and cushion the joint in order to reduce pain, stiffness and swelling caused by osteoarthritis when the patient has not responded to more conservative treatment;

- Chlorzoxazone caplets (*e.g.*, Parafon Forte and Lorzone, both of which have been discontinued in the U.S., but generic equivalents remain available), used to treat muscle spasms and musculoskeletal pain; and

- Metaxalone, (*e.g.*, Skelaxin, Metaxall), a tablet which is used as a muscle relaxant and to relieve pain caused by strains, sprains, and other musculoskeletal conditions.

Unlike other drugs discussed in this study, viscosupplements are not dispensed medications – they are physician-administered preparations, so they are not covered by the Formulary, which only applies to dispensed drugs. Furthermore, the pre-filled syringes are subject to "J-Code" payment rules for surgical injections included in the Physician Services and Non-Physician Practitioner Services section of the Official Medical Fee Schedule[6] rather than the Pharmacy Fee Schedule which uses NDC codes to identify specific drugs. The J-Codes bundle the cost of the drug with the professional service cost for the injection, but physicians often submit unbundled bills with separate charges for the injection service and an NDC for the cost of the drug. In many cases, these bills are paid, and since CWCI's drug data is based on NDC codes included in pharmaceutical bills, the viscosupplement data in the study only reflects prescriptions and payments for the hyaluronic acid preparations that were billed under NDC codes and excludes those billed under J-Codes.

Exhibit 3: % of 2021 Musculoskeletal Prescriptions and Musculoskeletal Payments



As noted in Exhibit 3, the NDC data show that viscosupplements accounted for just 3.5 percent of all California workers' compensation Musculoskeletal prescriptions in 2021, but with an average payment of $688, they consumed 43.7 percent of the Musculoskeletal dollars, more than cyclobenzaprine, tizanidine HCl, baclofen, methocarbamol, and carisoprodol combined.

[6] Injection codes for viscosupplements include: J7320, J7321, J7322, J7323, J7324, J7325, J7326, J7327, J7328.

Viscosupplements' share of the Musculoskeletal prescriptions declined from 2.6 percent in 2012 to 1.6 percent in 2015, then edged up to 1.8 percent by 2017, but after the state incorporated revised treatment guidelines for knee disorders into the MTUS in December 2017, that share rose to 2.6 percent in 2018, 2.7 percent in 2019 and 2020, then climbed to a 10-year high of 3.5 percent in 2021.

Until 2019, all viscosupplements used in workers' compensation were brand varieties, and brand-name products continued to dominate the market in 2021, when they again accounted for 100 percent of all viscosupplements administered to injured workers. Given the dominance of the brand varieties, average payments for viscosupplements have always been relatively high compared to other Musculoskeletal prescriptions, but they did fluctuate from a low of $385 in 2012 to a 10-year high of $726 in 2019 before retreating to $688 in 2021 as the mix of formulations used to treat injured workers shifted.

With these year-to-year fluctuations in the average payments and the shifts in their share of the Musculoskeletal prescriptions, the viscosupplements' share of the Musculoskeletal payments has ranged from 12.4 percent in 2014 to the record 43.7 percent in 2021. The most notable change in their share of the musculoskeletal drug payments was in 2018, when viscosupplement payments nearly doubled from 16.3 to 31.1 percent of the reimbursements within their drug group – the combined effect of their share of the prescriptions increasing from 1.8 to 2.6 percent after the Knee Disorder Guidelines were adopted and the $108 increase in their average reimbursement from $543 to $651.

Exhibit 4: Utilization and Payment 10-Year Growth Trends, Musculoskeletal Cost Drivers

Drug	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Viscosupplements										
% of Musculoskeletal Rx	2.6%	2.5%	1.7%	1.6%	1.7%	1.8%	2.6%	2.7%	2.7%	3.5%
Avg Paid	$385	$499	$510	$616	$476	$543	$651	$726	$697	$688
% of Musculoskeletal $	15.7%	14.2%	12.4%	13.9%	12.7%	16.3%	31.1%	39.2%	30.8%	43.7%
Chlorzoxazone										
% of Musculoskeletal Rx	0.5%	0.5%	0.5%	0.4%	0.5%	0.3%	0.5%	0.4%	0.9%	0.3%
Avg Paid	$17	$36	$99	$164	$224	$178	$502	$717	$1,442	$779
% of Musculoskeletal $	0.1%	0.2%	0.6%	0.9%	1.6%	0.8%	4.5%	6.1%	21.8%	4.9%
Metaxalone										
% of Musculoskeletal Rx	2.9%	2.8%	2.6%	2.4%	3.2%	4.6%	2.1%	2.1%	3.1%	4.2%
Avg Paid	$232	$233	$222	$201	$127	$117	$95	$95	$134	$160
% of Musculoskeletal $	10.2%	8.0%	8.1%	6.5%	6.3%	9.0%	3.7%	4.0%	6.8%	12.3%

The muscle relaxant chlorzoxazone works on the brain and spinal cord to prevent the generation of chemicals that cause pain in skeletal muscles and is used to treat patients with acute pain from muscle spasms when rest and physical therapy are not enough. Approved by the FDA in 1958, it has been used

in workers' compensation for decades, but as noted in Exhibit 4, since 2012 it has only represented between 0.3 percent and 1.0 percent of the Musculoskeletal Drugs used to treat injured workers.

While brand versions of the drug (Paraflex, Strifon Forte DSC) have been taken off the market in the U.S., generic chlorzoxazone is still available. Chlorzoxazone is listed as a Non-Exempt drug in the formulary, so it is subject to prospective UR, and under the formulary rules, unless the prescriber provides a rationale for using the brand version of the drug, the generic should be prescribed. As a result, since 2016 the brand versions have dwindled from 62 percent of the workers' compensation chlorzoxazone prescriptions to 0 percent in both 2020 and 2021. However, the biggest determinate of the price of this drug has not been whether a brand or generic version has been used, but the dosage, as the 500 mg tablets are relatively inexpensive, with some prescriptions costing less than $15, while other dosages (250 mg, 375 mg, and 750 mg) are much higher, with some costing well over $1,000, even when dispensed as a generic.

Over the past decade, prescriptions for dosages other than the low-cost 500 mg chlorzoxazone have become more prevalent in workers' compensation, as the average amount paid per chlorzoxazone prescription soared from $17 in 2012 to $779 in 2021. Most of that increase took place in the last five years, when average reimbursements increased nearly 8-fold, climbing from $178 in 2017 to a peak of $1,442 peak in 2020, which was also the year that chlorzoxazone's share of the Musculoskeletal prescriptions rose to a record 0.9 percent. Thus, 2020 was also the year that chlorzoxazone's share of the Musculoskeletal Drug spend hit an all-time high of 21.8 percent. Although chlorzoxazone's share of the Musculoskeletal prescriptions dropped back down to 0.3 percent in 2021 and the average payment fell to $779, it still represented 4.9 percent of the Musculoskeletal Drug spend that year.

Metaxalone is another low-volume/high-payment Musculoskeletal Drug, which like chlorzoxazone, has no direct effect on muscle tissue, but blocks nerve impulses in the brain and is used in conjunction with rest and physical therapy to treat injured workers suffering from muscle spasms and acute painful musculoskeletal conditions such as strains and sprains. In 2021, metaxalone accounted for 4.2 percent of the Musculoskeletal Drugs dispensed to California injured workers, but with an average reimbursement of $160 per prescription, it consumed 12.3 percent of the Musculoskeletal Drug spend.

Over the 10-year study period, metaxalone's share of the Musculoskeletal prescriptions fluctuated between 2.1 percent and 4.6 percent. Both brand-name (Skelaxin) and generic versions of the drug were available during that time, but brand versions dwindled from 14 percent of the metaxalone dispensed to injured workers in 2012 to 1 percent in 2016, and since then only generic versions have been used in workers' compensation.

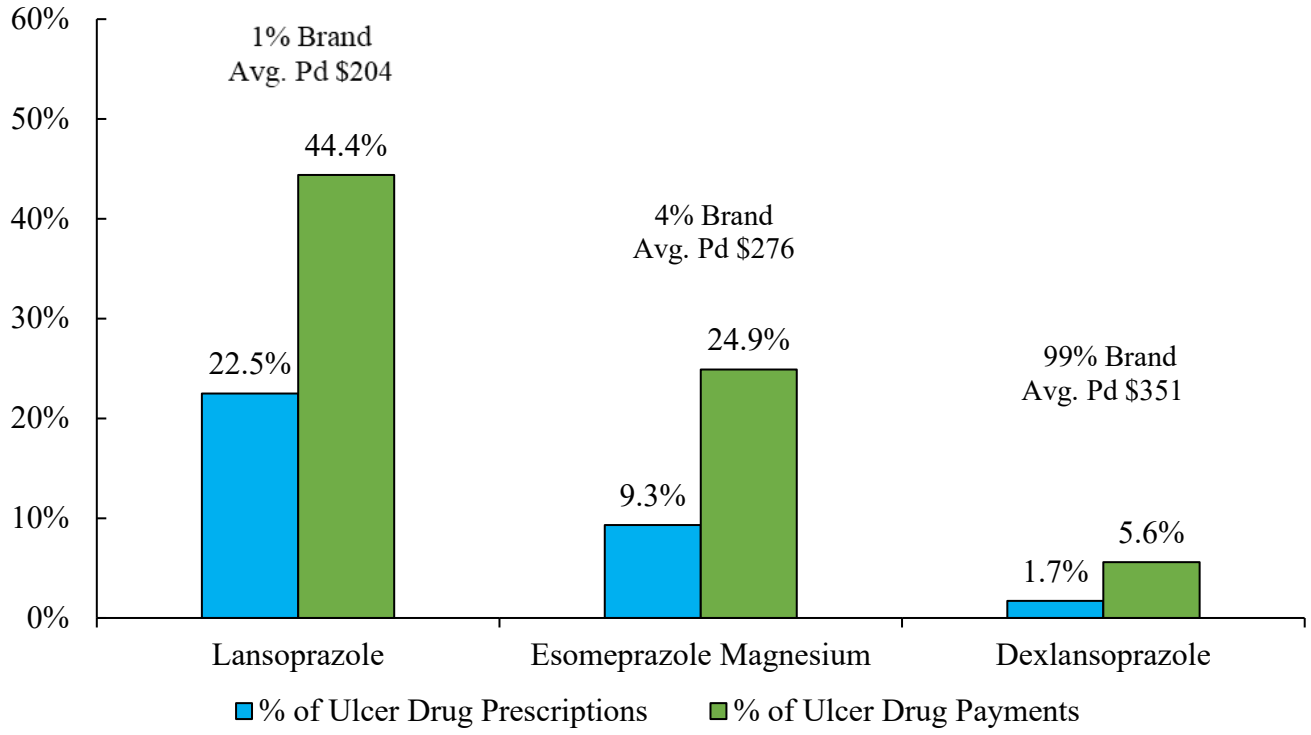
The average reimbursement per prescription for brand versions of metaxalone peaked at $514 in 2015, compared to $197 for the generics, but after the generics took over the market in 2016, the average payments gradually declined to $95 in 2019 before climbing back up to $134 in 2020 and $160 in 2021. A review of the dispensing data from those two years indicates that most of the recent increase in the average payments for metaxalone has been driven by physicians dispensing out of their offices and clinics. The growth in the average amount paid for metaxalone between 2019 and 2021 also coincided

with a doubling in its share of the Musculoskeletal prescriptions over the same two-year period, as it went from 2.1 percent to 4.2 percent of the prescriptions within its drug group.

Ulcer Drugs

Ulcer Drugs are often used to treat digestive issues related to Opioid and NSAID use. Since 2018 they have been the seventh most common drug category used in California workers' compensation, though with the declining use of opioids, their percentage of workers' compensation prescriptions has steadily declined from an all-time high of 7.3 percent in 2013 and 2014 to 5.4 percent in 2021. In terms of payments, Ulcer Drugs' share of the workers' compensation total drug spend declined from 10.0 percent in 2012 to 5.6 percent in 2018 as opioid utilization declined and the average amount paid per prescription fell from $158 to $84, but since then Ulcer Drug payments have represented an increasing share of the prescription drug spend, climbing back up to 6.5 percent in 2021 as the average amount paid for this category of drug climbed from $84 to $103.

Exhibit 5: % of 2021 Ulcer Drug Prescriptions and Ulcer Drug Payments



Relatively inexpensive Omeprazole (*e.g.,* Prilosec), which is widely available in generic forms, accounts for close to half of the Ulcer Drug prescriptions in California workers' compensation (47.8 percent in 2021), but with an average payment of $29 per prescription, it represented just 13.3 percent of the 2021 ulcer drug payments. On the other hand, as shown in Exhibit 5, three other high-priced Ulcer Drugs, lansoprazole (*e.g.,* Prevacid, average payment $204), esomeprazole magnesium (*e.g.,* Nexium, average payment $276), and dexlansoprazole (*e.g.,* Dexilant, average payment $351) accounted for a third of the Ulcer Drugs prescribed to injured workers in 2021 but nearly three quarters of the ulcer drug payments.

All of these Ulcer Drugs are classified as Exempt medications in the formulary, so they can be prescribed without prospective UR.

Exhibit 6: Utilization and Payment 10-Year Growth Trends, Ulcer Drug Cost Drivers

Drug	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Lansoprazole										
% of Ulcer Drug Rx	2.2%	2.2%	2.0%	2.6%	3.6%	10.0%	13.8%	12.8%	21.4%	22.5%
Avg Paid	$174	$174	$180	$227	$204	$296	$262	$251	$215	$204
% of Ulcer Drug $	2.4%	2.5%	2.3%	3.8%	7.7%	30.1%	42.9%	34.9%	49.0%	44.4%
Esomeprazole Magnesium										
% of Ulcer Drug Rx	3.4%	3.6%	3.2%	3.2%	3.8%	4.6%	5.2%	5.3%	6.6%	9.3%
Avg Paid	$239	$263	$295	$251	$201	$199	$154	$201	$237	$276
% of Ulcer Drug $	5.2%	6.0%	6.2%	5.2%	8.0%	9.2%	9.5%	11.6%	16.8%	24.9%
Dexlansoprazole										
% of Ulcer Drug Rx	1.1%	1.4%	1.8%	2.0%	1.7%	1.7%	1.6%	1.3%	1.3%	1.7%
Avg Paid	$150	$175	$209	$239	$261	$277	$315	$358	$380	$351
% of Ulcer Drug $	1.0%	1.6%	2.4%	3.1%	4.7%	4.9%	6.0%	5.0%	5.3%	5.6%

The first of the three cost-driver Ulcer Drugs identified in the Institute data, lansoprazole (*e.g.*, Prevacid) is a proton pump inhibitor – a drug that reduces the amount of acid produced in the stomach. In workers' compensation it is typically dispensed in 15 or 30 mg delayed release capsules to reduce the risks of ulcers developing in the stomach or intestines, or to treat acid reflux and heartburn in patients who take NSAIDs or Opioids. The utilization data show that from 2012 through 2016, lansoprazole represented between 2.0 percent and 3.6 percent of the Ulcer Drug prescriptions dispensed to injured workers, but in 2017 that percentage jumped to 10.0 percent, then more than doubled over the next four years, climbing to 22.5 percent in 2021.

Much of that increase occurred in 2020, when lansoprazole's share of the Ulcer Drugs climbed from 12.8 percent to 21.4 percent – an increase that coincided with the FDA's removal of the popular ulcer drug ranitidine (Zantac)[7] from the U.S. market due to cancer concerns. In 2019, ranitidine had accounted for 10.5 percent of the Ulcer Drug prescriptions, but because it was relatively cheap (averaging $55 per prescription) it only consumed 6.3 percent of the 2019 Ulcer Drug payments. The sudden surge in the use of lansoprazole in 2020 suggests that as soon as ranitidine was pulled from the market, physicians started prescribing much more expensive lansoprazole (which averaged $215 per

[7] In April 2021, a new over-the-counter ulcer drug called Zantac 360 that contained the same active ingredient as Pepcid and Pepcid AC (Famotidine) instead of Ranitidine was released. Medications containing Famotidine peaked at 12.3 percent of ulcer drug prescriptions and 7.9 percent of ulcer drug payments in 2019, though they still represented 10.1 percent of the prescriptions and 4.1 percent of the payments in service year 2021.

prescription), and as a result, that year lansoprazole went from 34.9 percent to 49.0 percent of the Ulcer Drug payments.

The data on lansoprazole show that the use of generics does not necessarily reduce costs. From 2012 through 2016, use of brand versions of lansoprazole fell sharply, declining from 10 percent of the prescriptions in 2012 to 4 percent in 2016, but in 2017, the same year that lansoprazole's share of the Ulcer Drug prescriptions nearly tripled, brand versions of the drug fell to just 2 percent of the prescriptions for this medication, then declined to 1 percent in 2018 where it has remained ever since. A closer review of the prescription data reveals that most of the generic lansoprazole dispensed in recent years has come from a single manufacturer, and in a majority of the cases, it has been dispensed directly by the physician or clinic treating the injured worker, rather than by a pharmacy. Furthermore, beginning in 2015, there was a notable shift away from the 30 mg lansoprazole prescriptions, which had been the dominant dosage prescribed to injured workers, toward more expensive 15 mg prescriptions, with the same single manufacturer seeing its share of the 15 mg prescriptions increase from 0.7 percent in 2015 to 22.8 percent in 2016, 74.3 percent in 2017, and 80.5 percent in 2018, suggesting a major promotional push toward physician dispensing of the 15 mg prescriptions of this medication.

The second cost driver Ulcer Drug identified by the Prescription Drug Application, esomeprazole magnesium (*e.g.,* Nexium), is another proton pump inhibitor. Like lansoprazole, it reduces acid in the stomach and is used to treat heartburn, acid reflux, and to help prevent ulcers in patients taking NSAIDs and Opioids, but it lasts longer than lansoprazole. Low-dose (20 mg) versions of the drug are available over the counter and as prescription generic and brand tablets and capsules, while the higher dosage (40 mg) versions require a prescription.

From 2012 through 2015, esomeprazole magnesium represented 3.2 percent to 3.6 percent of the Ulcer Drugs prescribed in California workers' compensation, but it wasn't until August of that year that the first generic version of the drug became available. With the release of generic esomeprazole magnesium, utilization of the medication began to increase and in 2016 its share of the Ulcer Drugs dispensed to injured workers rose to 3.8 percent, then continued to climb over the next five years, hitting a record 9.3 percent in 2021. Generics quickly came to dominate the market, representing 68 percent of the workers' compensation prescriptions in 2015, then increasing each year thereafter, hitting a record 96 percent of the esomeprazole magnesium prescriptions in 2021.

Meanwhile, the payment data show that the average reimbursement for an esomeprazole magnesium prescription rose 23.4 percent from $239 in 2012 to $295 in 2014, but following the introduction of the generics, that average fell 47.8 percent to $154 in 2018. Since 2018, however, the average payments have increased steadily, climbing 79.2 percent to $276 in 2021. As with lansoprazole, the payment data show some of this increase can be ascribed to physician dispensing, though there is also a wide variation in the average amounts paid for generic versions of the drug. With the growing utilization of esomeprazole magnesium following the introduction of the generics, and the recent escalation in the average payment for the drug, this drug's share of the Ulcer Drug payments has more than tripled from 8.0 percent in 2016 to 24.9 percent in 2021, with most of that increase occurring as the average payments increased from 2018 through 2021.

A third proton pump inhibitor, dexlansoprazole (*e.g.*, Dexilant), is another low-volume, high-cost Ulcer Drug that represented 1.7 percent of the prescriptions within this drug group in 2021, but with an average payment of $351 per prescription, it was the highest-cost drug within this category and accounted for 5.6 percent of the 2021 Ulcer Drug payments.

Dexlansoprazole is a dual delayed-release drug that combines two different granules within a single 30 or 60 mg capsule, allowing an initial release of the medication in the stomach within an hour of ingestion, and a second release of the medication in the small intestine 4 to 5 hours later. Initially approved by the FDA in January 2009, and only available by prescription, dexlansoprazole is used to treat acid reflux, esophogheal erosion, and ulcers. The FDA approved a generic version of the drug in May 2017, but the generic did not become widely available until January 2022, so it was the last remaining single-source (brand) proton pump inhibitor on the market, and the brand version has comprised nearly 100 percent of the dexlansoprazole dispensed to injured workers since 2012.

The 10-year utilization trend for dexlansoprazole shows its share of Ulcer Drug prescriptions nearly doubled from 1.1 percent in 2012 to a peak of 2.0 percent in 2015, then gradually tapered down to 1.3 percent in 2020 before rebounding to 1.7 percent in 2021. On the other hand, dexlansoprazole's share of the Ulcer Drug payments increased six-fold between 2012 and 2018, climbing from 1.0 percent to 6.0 percent, then edging down slightly to between 5.0 percent to 5.6 percent of the Ulcer Drug dollars from 2019 through 2021. From 2012 to 2020, the average amount paid per dexlansoprazole prescription rose steadily, more than doubling from $150 to $380 before dipping slightly to $351 in 2021.

The factors fueling the growth in the average dexlansoprazole payments differ from those that drove up the payments for the other two high-priced/low-volume proton pump inhibitors. Unlike lansoprazole, very little if any dexlansoprazole has been physician dispensed, and unlike both lansoprazole and esomeprazole magnesium, generic versions of the drug were not widely available until last year. The key factors affecting the average amounts paid for dexlansoprazole prescriptions are the growth in the average number of capsules per prescription, which increased by about 50 percent from 2012 to 2020, and the fact that until very recently, this medication has only been available as a single-source brand drug, so while less expensive alternatives have been on the market, less expensive generic versions of this drug have not, so the average reimbursement for dexlansoprazole has remained relatively high compared to other Ulcer Drugs.

Discussion

This report, and the two others in the research series, document shifts in prescription drug utilization and payments in California workers' compensation from 2012 through 2021. To a great extent, these shifts were driven by changes enacted over the past 20 years, including mandatory utilization review and the adoption of independent medical review to resolve medical disputes and assure that drugs used to treat injured workers are appropriate, safe, and efficacious; the growth of medical provider networks that set physician-dispensing rules for plan providers and that contract with pharmacy benefit managers; the implementation of the Pharmacy Fee Schedule and subsequent changes in the Medi-Cal Fee Schedule on

which it is based. At the same time, changes in the types of drugs dispensed have reflected a growing public awareness of the risks associated with the long-term use of opioids and other addictive medications; increased reliance on generics; and more recently, the adoption of Chronic Pain and Opioid Treatment Guidelines into the MTUS and the 2018 implementation of the MTUS Formulary.

This research series has provided multiple examples of high-cost medications that account for just a small share of the prescriptions within their drug group that have become significant cost drivers. For example, the three Musculoskeletal Drugs identified in this report, viscosupplements, chlorzoxazone, and the metaxalone, together accounted for just 8.0 percent of Musculoskeletal prescriptions in service year 2021, but 60.9 percent of the Musculoskeletal Drug payments; while the three Ulcer Drugs, lansoprazole, esomeprazole magnesium, and dexlansoprazole, together represented 33.5 percent of the Ulcer Drug prescriptions dispensed to injured workers in 2021, but 74.9 percent of the Ulcer Drug payments. While the use of low-volume/high-cost drugs to treat injured workers may be appropriate if they have been shown to cure or relieve the effects of a work-related injury, in many cases, less expensive versions of the same or similar medications are available, so payers and providers should make sure there is a sound, evidence-based rationale for prescribing them, and be fully aware of the alternatives that are available.

As has been evident throughout this research series, total payments within a drug group depend on a variety of factors that extend beyond the volume of prescriptions. These include the mix of drugs within the group; the fees allowed under the Pharmacy Fee Schedule; the average quantities and dosages dispensed; the mode of delivery; whether the medications are dispensed by a physician, clinic, or pharmacy; whether the prescriptions are for extended-release or tamper-resistant versions of the drugs; and the availability of generic or over-the-counter versions of the drugs or appropriate alternatives. In addition, since the Formulary took effect, the number of prescriptions and the total amounts paid for each drug group have been affected by the extent to which drugs within the group have been Exempt or Non-Exempt from prospective utilization review (UR), not listed in the Formulary (making them subject to prospective UR), or have been included in the Formulary's "special fill" or "perioperative" categories that allow restricted use.

Notably, the Formulary is subject to regular review by the DWC's Pharmacy and Therapeutics (P&T) Committee and since it took effect five years ago, its drug lists have been revised multiple times to reflect changes in the MTUS Guidelines. The most recent revision was Version 10, which took effect November 1, 2022. The P&T Committee also reviews issues related to prescription drugs and has already suggested adding "Dosage Form," "Strength," and "Unique Pharmaceutical Identifier" to the drug list to further identify drugs as Exempt or Non-Exempt based on the form of dosage and strength for the same drug ingredient – which would allow more nuanced Exempt status designations for drugs at safe dosages, helping to curb the use of special formulations to increase reimbursement – an issue that this research shows remains problematic given the impact of low-volume, high-priced drugs that lack price controls and are exempt from prospective UR.

The prescription drug market is constantly evolving as new drugs are introduced, older medications are retired or reformulated, patents on brand drugs expire and generic versions hit the market, and revisions

are made to the MTUS Formulary. As these changes CWCI will continue to monitor the utilization and reimbursement of prescription drugs in California workers' compensation both in future reports and in updates to our Prescription Drug Interactive Data Application and our Formulary Interactive Data Application, which CWCI members can access by logging on to our website at www.cwci.org and clicking Interactive Research Tools under the Research tab.

About the Authors

Bob Young is the Communications Director at the California Workers' Compensation Institute.

Stacy L. Jones is a Senior Research Associate at the California Workers' Compensation Institute.

Acknowledgements

The authors would like to thank CWCI Senior Research Associates Steve Hayes and Robby Bullis for their input and contributions in the development of the prescription drug data used for this research series and in the preparation of this report.

California Workers' Compensation Institute

The California Workers' Compensation Institute, incorporated in 1964, is a private, nonprofit organization of insurers and self-insured employers conducting and communicating research and analyses to improve the California workers' compensation system. Institute members include insurers that collectively write 79% of California workers' compensation direct written premium, as well as many of the largest public and private self-insured employers in the state. Additional information about CWCI research and activities is available on the Institute's website (www.cwci.org).

CWCI Spotlight Reports are published by the California Workers' Compensation Institute.

1999 Harrison St., Suite 2100, Oakland, CA 94612
https://www.cwci.org

510-251-9470