California Workers' Compensation Institute

Spotlight Report

Cost-Driver Medications in the Top California Workers' Comp Therapeutic Drug Groups, Part II: Dermatologicals, Opioids, and Antidepressants

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Background

This report is the second in a 3-part series that examines prescription drugs that are currently used in California workers' compensation that account for a relatively small share of the prescriptions within their therapeutic drug group, but a relatively high share of the payments. The research series is based on data from the January 2023 version of the CWCI Prescription Data Application,[1] which contains data on medications dispensed to California injured workers between January 2007 and June 2022. The most recent full-year data in the application showed that there were seven therapeutic drug groups that accounted for at least 5 percent of the workers' compensation prescriptions filled in 2021: Anti-Inflammatories; Anticonvulsants; Dermatologicals; Opioids; Antidepressants; Musculoskeletal drugs; and Ulcer drugs. Combined, these seven drug groups represented 82.3 percent of the workers' compensation prescriptions in service year 2021, and 69.2 percent of the total drug spend.[2]

In March 2021, a CWCI analysis of California workers' compensation prescription drug utilization and payment trends noted that in the first half of service year 2020, Anti-Inflammatories accounted for more than a third of all prescription drugs dispensed to California injured workers -- three times the proportion noted for Opioids, which ranked second.[3] The study also noted that even though most of the Anti-Inflammatories were inexpensive and utilization had been flat since the implementation of the Medical Treatment Utilization Schedule (MTUS) Formulary in 2018, Anti-Inflammatories' share of the total drug spend had increased from 14.2 percent to 23.5 percent, an increase largely driven by payments for two low-volume, high-priced drugs: fenoprofen calcium and ketoprofen, which are used to treat arthritis and pain. A closer review found that the MTUS Formulary classifies both fenoprofen calcium and ketoprofen as Exempt drugs, so they are not subject to prospective utilization review (UR), and since neither is in the national Medicaid database, they had no Federal Upper Limit (FUL) which would have served as a price control in workers' compensation.

That finding sparked questions as to the extent to which low-volume/high-cost drugs in other drug groups may have become cost drivers. To investigate, the Institute initiated additional research that began with a review of Dermatological drugs, which had become the second most expensive drug group

[1] CWCI's Prescription Drug Application is an online tool available to CWCI members at https://www.cwci.org/ClaimMonApp.html
[2] Service year refers to the calendar year (January 1 through December 31) in which a prescription was dispensed.
[3] Young, B., Secia, J. and Hayes, S. *California Workers' Compensation Prescription Drug Trends.* CWCI Research Update, March 2021.

behind Anti-Inflammatories, representing 17.3 percent of the total drug spend in 2021, even though they ranked fourth in terms of workers' compensation prescription volume, accounting for 9.3 percent of the dispensed prescriptions. The relatively high share of dollars flowing to Dermatologicals suggested that some of these medications are very expensive, and a review of the average payment data confirmed that this was indeed the case, identifying a fairly new drug, Xrylix, as another low-volume, very high-priced medication that had become a major cost driver within the Dermatological drug group.

Xrylix, a topical medication used to treat arthritis of the knee, is dispensed as a kit containing a diclofenac sodium solution and adhesive sheets, and it is ***not*** FDA approved. Furthermore, a review of the billing information revealed it had only been dispensed by a handful of small pharmacies. As with fenoprofen calcium and ketoprofen, Xrylix is not in the national Medicaid database and has no FUL to control the price, so it is reimbursed at 83 percent of the average wholesale price (AWP), which is based on manufacturer pricing. In 2021, California workers' compensation claims administrators paid an average of $4,126 per prescription for Xrylix (close to what has been paid since 2017 when it first appeared in the data), so even though it only represented 0.3 percent of workers' compensation Dermatological scripts, it consumed 7.2 percent of Dermatological dollars.

Further analysis of the Dermatological drugs in CWCI's Prescription Drug Application revealed other examples of high-priced kits containing topical medications that were dispensed in 2021, including Diclovix, a diclofenac sodium solution with camphor-lidocaine-methyl salicylate patch kit, which had an average payment of $1,631; and Prilovix Ultralite Plus, which consists of a tube of lidocaine-prilocaine cream, an occlusive dressing, and some scissors, and had an average reimbursement of $3,080.

Given the impact that these low-volume Dermatologicals had on the total drug spend for their group, the authors decided to conduct additional reviews of the Prescription Data Application to see if other drugs in the seven most heavily used therapeutic drug groups had an outsized impact on drug costs within their drug categories and to highlight the results in a research series. Part I of the series examined Anti-Inflammatory and Anticonvulsant medications; this report focuses on additional Dermatological drugs, Opioids, and Antidepressants; and Part III will look at Musculoskeletal and Ulcer drugs.

Data and Methods

CWCI's Prescription Drug Application contains detailed data on California workers' compensation prescriptions extracted 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.

[4] IRIS is CWCI's proprietary transactional database of insured and self-insured policies and their associated claims. Version 2022A, 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 Kluwers Health, Medi-Span.

The January 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 of 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 represented at least 5 percent of the service year 2021 prescriptions. As previously noted, seven therapeutic drug groups had at least a 5 percent share of the California workers' compensation prescriptions dispensed in 2021, and no other drug groups represented more than 2.1 percent of the prescriptions.

Individual drugs within the top seven drug groups were ranked based on their percentage of the 2021 total prescriptions and payments within their 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 were based on service year 2012 through service year 2021 prescription data, reported as of June 30, 2022.

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 MTUS Formulary. Therefore, to identify drugs that are currently consuming a disproportionately high share of the total dollars paid within their drug group, the authors focused on medications dispensed in service year 2021 (the most recent full-year data included in the Prescription Data Application).

The authors also used the service year data to note changes in the average amount paid per prescription for each drug within the 10-year study period, and the percentage that were dispensed as brand drugs rather than as generics. IRIS data was used to identify the manufacturer of the drug, where the prescriptions were dispensed, the form, dosage, and quantity of the drug dispensed, and additional pricing information.

Objective

The goal of the research series is to identify relatively low-volume/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). In addition, each report in the series examines factors that may have driven up the cost of these drugs and the extent to which those factors may be better controlled. Service year 2021 data from the January 2023 version of the CWCI Prescription Drug Application was used to identify:

- Each drug's share of the prescriptions and payments within their therapeutic drug group;
- The average amount paid per prescription for each of the drugs; and
- The percentage of the prescriptions for each drug that were dispensed as brand vs. generic.

The report also uses data from service years 2012 through 2021 to show:

- How each drug's share of the prescriptions within its therapeutic drug group changed over that 10-year span;
- How each drug's share of the payments within its therapeutic drug group changed over the 10-year span; and
- How the average amount paid per prescription changed.

Findings

Exhibit 1 shows the top seven drug groups, which together accounted for 82.3 percent of the prescriptions dispensed to injured workers in 2021 -- a percentage has been fairly stable since 2012 (ranging from 81.1 percent to 83.7 percent). Over the 10-year span of the study, Opioids' share of the workers' compensation prescriptions have registered the biggest drop, falling from 29.4 percent in 2012 to 9.4 percent in 2021, followed by Musculoskeletal drugs, which declined from 9.7 percent to 5.9 percent of the prescriptions. On the other hand, Anti-Inflammatories had the biggest increase, climbing from 17.7 percent to 34.8 percent of the prescriptions, while Anticonvulsants jumped from 5.5 percent to 9.6 percent and Dermatologicals increased from 5.8 percent to 9.3 percent.

Notably, Antidepressants' share of the prescriptions rose from 5.9 percent in 2012 to 7.9 percent in 2021, with much of that increase after the Pain Management and Opioid Guidelines took effect in 2018 and then continuing during 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

As noted in Exhibit 2, the sharp decline in Opioid utilization and the increase in the use of Anti-Inflammatories and other types of drugs that are often prescribed for off-label use as non-opioid analgesics also led to a significant redistribution of workers' compensation pharmaceutical payments over the 10-year study period.

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 workers' compensation drug spend in 2012 to just 5.8 percent in 2021, Anti-Inflammatories' share 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. Part I of this research series[6] found that Anticonvulsants have represented a declining share of the payments since 2019, which coincides 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 drug (Lyrica). Drug categories that saw their share of the total drug spend decline over the decade included Ulcer drugs (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, and Musculoskeletal drugs, which declined from 5.6 percent to 3.7 percent.

At the same time that the prescription and payment distributions among top drug groups were shifting, changes were also occurring within each group as new medications, formulations, and products were introduced, patents on brand drugs expired and generic versions became available, and older drugs 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 third, fourth, and fifth most heavily utilized drug groups: Dermatological drugs, Opioids, and Antidepressants. Each section reviews the most significant "cost-driver" medications that were found within the group, including their 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.

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

Dermatologicals

CWCI's latest update to its Prescription Data Application shows that Dermatological drugs were the fourth most prevalent drug category in California workers' compensation in 2021, accounting for 9.3 percent of all medications dispensed to injured workers. At the same time, Dermatological drugs now rank second in terms of drug payments, consuming 17.3 percent of the total drug spend. Data in the application traced much of the growth in the Dermatological drug spend over the past 13 years to increased utilization, as Dermatologicals accounted for an increasing share of workers' compensation prescriptions as the use of Opioids declined. However, the application also revealed that the surge in Dermatological payments coincided with a change in the mix of Dermatological drugs, most notably with the emergence of high-priced topical analgesics.

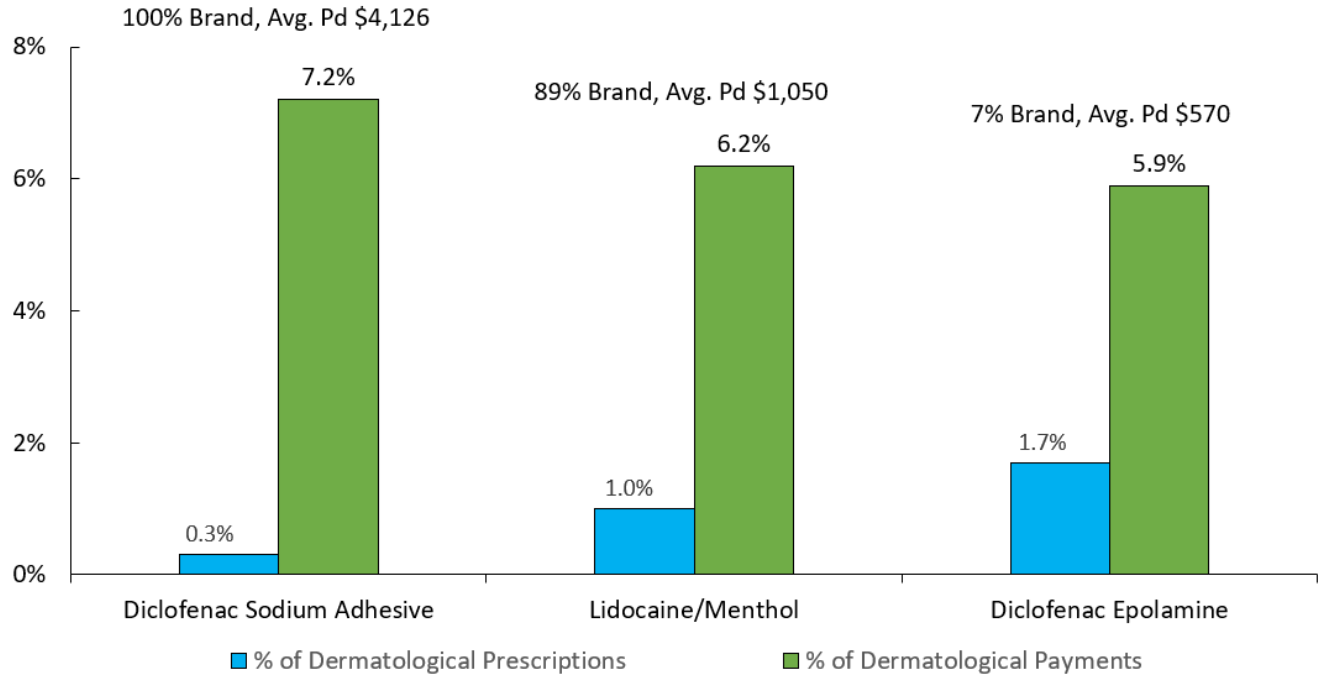
Among the topical analgesics that have seen dramatic growth over the past decade are diclofenac sodium topicals, which are NSAID gels and creams used to treat pain due to arthritis and joint inflammation. Prior to 2016, most of the diclofenac sodium topicals used in workers' compensation were brand varieties, but since then a wide variety of generic formulations and products have been introduced, and they now dominate the market, with generics increasing from 2 percent of the diclolfenac sodium topicals in 2015 to 60 percent in 2016, 95 to 98 percent from 2017 to 2019, and 99 percent in 2020 and 2021.

Within the past decade, diclofenac sodium topicals increased from 0.5 percent of all workers' compensation prescriptions in 2012 to 1.3 percent in 2017, but after they were categorized as Exempt drugs in the Formulary, they increased to 2.4 percent of the prescriptions in 2018, then climbed steadily to 5.4 percent in 2021, ranking fourth in terms of utilization among all drugs dispensed in workers' compensation. Measured as a proportion of the workers' compensation Dermatologicals, diclofenac sodium topicals nearly tripled from 8.2 percent in 2012 to 23.8 percent in 2017, after which that percentage soared to 58.1 percent in 2021.

Since 2020, diclofenac sodium topicals have been available over the counter or as prescriptions, but in 2021, 99 percent of the workers' compensation prescriptions for these medications were generics for which claims administrators paid an average of $60. In contrast, brand-name diclofenac sodium topicals dispensed to injured workers in 2021 averaged $611 per prescription, but prescriptions for brand versions were so rare that the overall average payment for this medication was a relatively low $65. As a result, even though diclofenac sodium topicals represented 58.1 percent of the Dermatological prescriptions dispensed in 2021, they accounted for only 23.5 percent of the total drug spend within this category.

On the other hand, as shown in Exhibit 3, three other medications that had much smaller shares of the 2021 dermatological prescriptions (the previously discussed diclofenac sodium adhesive sheets, along with lidocaine/menthol, and diclofenac epolamine) together accounted for 3.0 percent of the prescriptions within this drug group, but represented a much higher share of the payments, consuming 19.3 percent of last year's Dermatological drug spend.

Exhibit 3: Percentage of 2021 Dermatological Prescriptions and Payments



As noted earlier, the brand name for diclofenac sodium and adhesive sheets is Xrylix, which is a private label arthritis medication dispensed by a handful of pharmacies as a kit containing a diclofenac sodium solution and adhesive sheets. Xrylix is not listed in the Medicaid database and has no FUL, so workers' compensation claims administrators pay 83 percent of the AWP, which is based on manufacturer pricing. Since it first appeared in CWCI's pharmacy data in 2018, Xrylix has accounted for 100 percent of the diclofenac sodium and adhesives dispensed to injured workers, and as noted in Exhibit 4, over that four-year span average payments for these prescriptions ranged between $4,120 and $4,177, making this one of the most expensive Dermatological drugs used in workers' compensation. Xrylix's share of the Dermatological prescriptions more than doubled from 0.3 percent in 2018 to 0.7 percent in 2019, the same year the average payment peaked, which pushed its share of the Dermatological drug spend to a record 13.2 percent. In 2020 it fell to 0.2 percent of the prescriptions in this drug category before edging up to 0.3 percent in 2021, but with payments averaging $4,125 and $4,126 in those two years, it still consumed 5.8 percent and 7.2 percent of the Dermatological dollars respectively.

Lidocaine/menthol medications are combination drugs used for muscle and joint pain. They come in many different forms, including brand and generic versions of gels, ointments, creams, sprays and patches, and they are available both over the counter and as prescriptions. While many of these products are inexpensive, a review of the Institute's Pharmacy Application data shows two high-priced, private label prescriptions, NuLido gel and Terocin patches, are the primary lidocaine/menthol cost drivers in California workers' compensation. While single-ingredient lidocaine patches are in the MTUS formulary and were reclassified from Non-Exempt to Exempt effective November 1, 2022, neither NuLido nor Terocin are listed in the formulary, so they are subject to prospective UR, but can be

allowed if the treating physician can show that their use is supported by the MTUS or other guidelines. Payment records for these drugs show that although some are physician-dispensed, most are filled by smaller pharmacies or by mail-order dispensaries, with the typical reimbursement for NuLido averaging $422 and the reimbursements for Terocin averaging well over $1,000 per prescription for 30 patches.

In 2021, lidocaine/menthol medications accounted for 1.0 percent of the Dermatological prescriptions, but the average reimbursement of $1,050 suggests that Terocin represented a large share of them. Within the past decade, these medications climbed from 2.9 percent of the Dermatological prescriptions in 2013 to a peak of 7.4 percent in 2014, but that percentage began to trend down in 2015, with lidocaine/menthol drugs declining to just 0.9 percent of the Dermatological prescriptions in 2019, before edging up to 1.0 percent in 2020 and 2021. The historical payment data show that since 2013, average payments for lidocaine/menthol prescriptions ranged between a low of $633 in 2014 and a high of $1,050 in 2021, but the sharp decline in their share of the Dermatological prescriptions since 2014 helped offset the increase in the average paid per prescription, so lidocaine/menthol's share of the Dermatological drug spend fell from 16.4 percent in 2014 to 2.6 percent in 2019. In the two subsequent years, lidocaine/menthol's share of the Dermatological drug spend rose back up to 6.2 percent, largely due to a 64.3 percent increase in the average reimbursement, which climbed from $639 in 2019 to $1,050 in 2021.

The third Dermatological cost driver, diclofenac epolamine, is another NSAID topical medication that is used to treat acute pain from musculoskeletal injuries such as sprains, strains, and contusions. Dispensed as a transdermal patch (brand name Flector) that allows the drug to be absorbed at a fairly steady rate into the system (typically over a 12- to 14-hour period) while avoiding adverse effects, such as stomach issues, that can arise from ingesting NSAIDs. In 2021, diclofenac epolamine accounted for 1.7% of the Dermatological drugs dispensed to injured workers, but with an average reimbursement of $570, it consumed 5.9 percent of the Dermatological drug spend.

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

Drug	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Diclofenac Sodium and Adhesive Sheets										
% of Dermatological Rx	NA	NA	NA	NA	NA	NA	0.3%	0.7%	0.2%	0.3%
Avg Paid	NA	NA	NA	NA	NA	NA	$4,120	$4,177	$4,125	$4,126
% of Dermatological $	NA	NA	NA	NA	NA	NA	5.7%	13.2%	5.8%	7.2%
Lidocaine Menthol										
% of Dermatological Rx	NA	2.9%	7.4%	5.0%	4.3%	2.0%	1.3%	0.9%	1.0%	1.0%
Avg Paid	NA	$686	$633	$764	$731	$833	$735	$639	$717	$1,050
% of Dermatological $	NA	7.3%	16.4%	12.0%	9.6%	5.4%	4.0%	2.6%	4.8%	6.2%
Diclofenac Epolamine										
% of Dermatological Rx	7.1%	6.3%	6.0%	6.3%	5.3%	4.6%	4.2%	3.3%	2.5%	1.7%
Avg Paid	$284	$321	$341	$393	$446	$511	$565	$568	$559	$570
% of Dermatological $	8.2%	7.4%	7.2%	7.9%	7.3%	7.5%	10.0%	8.6%	8.9%	5.9%

As with fenoprofen calcium and ketoprofen, diclofenac epolamine is not listed in the national Medicaid database and has no FUL to control the price in California workers' compensation, and it is Unlisted by the MTUS Formulary. It was only available as a brand drug until 2019, when authorized generic versions were released by two manufacturers in the same strength as the Flector patch. The 10-year utilization data show that Flector patches accounted for as much as 7.1 percent of the workers' compensation Dermatological prescriptions in 2012, but by 2018, that share had dwindled to 4.2 percent. However, because the average amount paid per prescription had nearly doubled from $284 to $565 over that 7-year span, diclofenac epolamine's share of the Dermatological drug spend increased from 8.2 percent in 2012 to 10.0 percent in 2018.

Following the introduction of the authorized generics, Flector's share of the workers' compensation diclofenac epolamine prescriptions fell to 50 percent in 2019, 21 percent in 2020, and 7 percent in 2021. While average diclofenac epolamine payments have leveled off with the increased use of the authorized generics ($568 in 2019, $559 in 2020, and $570 in 2021), the authorized generics are also relatively expensive, with average payments of $573 in 2019, $535 in 2020, and $577 in 2021, so diclofenac epolamine remains one of most costly workers' compensation Dermatological drugs. Since 2018 its share of the Dermatological payments has declined from 10.0 percent to 5.9 percent, but that has been due more to diclofenac epolamine's declining share of the Dermatological prescriptions (from 4.2 percent to 1.7 percent) than to the introduction of authorized generics.

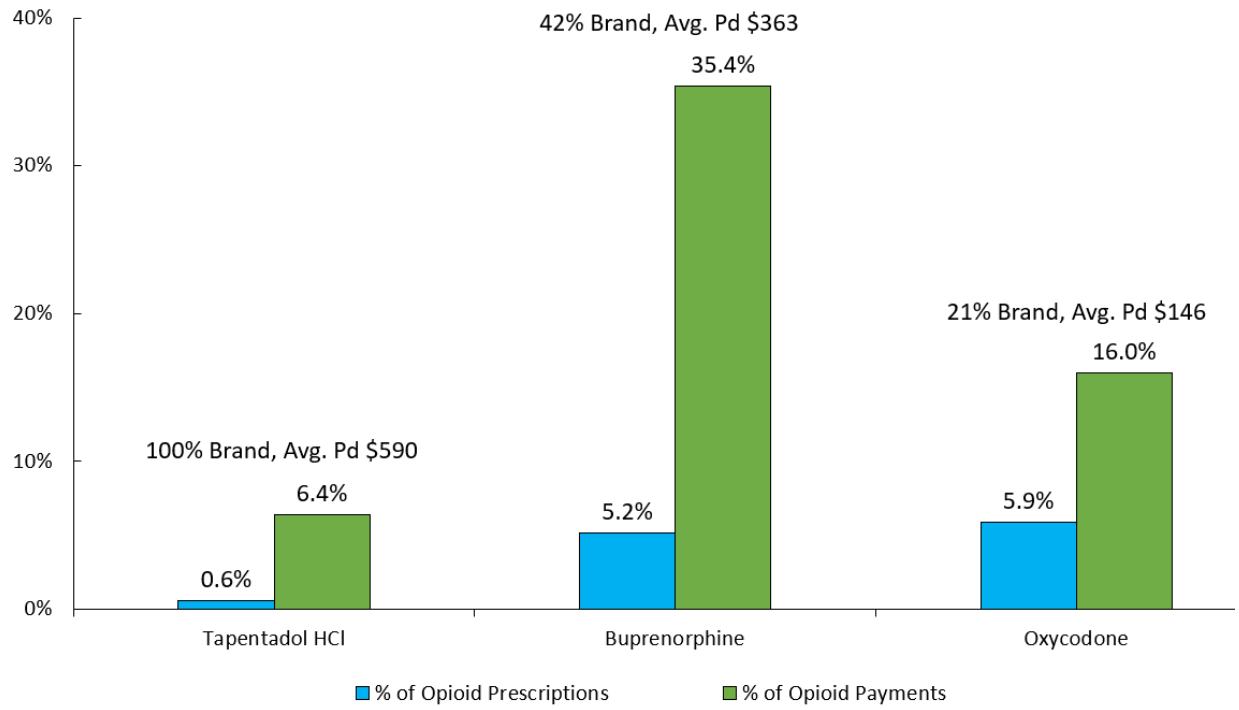
Opioids

When Opioid utilization peaked in 2009, these medications accounted for nearly a third of all prescription drugs dispensed to California injured workers, but their use has been declining steadily for more than a decade, though in 2021 Opioids still accounted for 9.4 percent of all workers' compensation prescriptions, making them the third most utilized drug group, just ahead of Dermatologicals, which accounted for 9.3 percent of the prescriptions.

According to the most recent data, hydrocodone with acetaminophen (*e.g.,* Vicodin), tramadol (*e.g,.* Ultram), and oxycodone with acetaminophen (*e.g*., Percocet) are the most heavily utilized Opioids in California workers' compensation. However, all three of these drugs are relatively inexpensive, with per prescription payments averaging $18, $28, and $41 respectively in 2021, so even though together they represented more than three-quarters of the Opioids dispensed in 2021, they represented just over a third of the payments (33.7 percent).

On the other hand, as noted in Exhibit 5, three lower volume, higher priced drugs, buprenorphine, tapentadol HCl, and oxycodone (often prescribed in the form of an extended-release, abuse-deterrent, drug), which together comprised only 11.7 percent of the Opioids prescribed to injured workers in 2021, consumed a much high share of the Opioid payments, accounting for 57.8 percent of the Opioid drug spend in 2021 year, making them significant cost drivers within the Opioid category.

Exhibit 5: Percentage of 2021 Opioid Prescriptions and Payments



Within the Formulary, tapentadol HCl, buprenorphine, and oxycodone are all categorized as Non-Exempt drugs which are subject to prospective UR. In addition, the Formulary lists oxycodone as a "Special Fill" drug, a four-day supply of which is exempt from UR if prescribed at an injured worker's initial visit that occurs within seven days of the injury date; and as a "Perioperative" drug, a limited supply of which may be prescribed without utilization review during the perioperative period, defined as four days prior to a surgery to four days after a surgery.

Tapentadol HCl is only available as a brand drug (Nucynta or Nucynta Extended Release). Because less costly generic versions are not available, the average price paid in 2021 was $590 per prescription, making it one of the most expensive Opioid drugs. Thus, even though tapentadol HCl accounted for only 0.6 percent of the Opioid prescriptions in 2021, it consumed 6.4 percent of the Opioid payments.

Buprenorphine, which is classified as a Schedule III drug as it has an accepted medical use in treatment and less potential for misuse or physical or psychological dependence than Schedule I and II drugs, is used to treat severe pain and Opioid Use Disorder (OUD) for patients in Medication-Assisted Treatment (MAT) plans, which typically run from six months to a year. Used within a MAT plan, buprenorphine has been shown to diminish the effects of withdrawal symptoms and reduce overdose deaths.[7]

In 2021, brand varieties accounted for 42 percent of the buprenorphine used in California workers' compensation, with average payments of $594 for brand buprenorphine prescriptions, more than triple

[7] Samples, H., Nowels, M., Williams, A. Olfson, M., Crystal, S. *Buprenorphine After Nonfatal Opioid Overdose: Reduced Mortality Risk in Medicare Disability Beneficiaries.* American Journal of Preventive Medicine, March 2023.

the $195 average for generic versions, which drove the overall average payment up to $363. Buprenorphine is available in tablet form, which tends to be less expensive, or as a film or patch, where depending on the quantity dispensed, average payments typically ranged from a few hundred dollars to more than $1,000 per prescription. With buprenorphine now widely used for MAT plans lasting 6 to 12 months, it accounted for 5.2 percent of the opioids dispensed in 2021 (fifth among all Opioids), but with its high average payment, it ranked first in terms of the Opioid drug spend, consuming 35.4 percent of the payments within this drug category. That was well ahead of hydrocodone-acetaminophen, which represented nearly half (47.9 percent) of the 2021 Opioid prescriptions but had an average reimbursement of $18 per prescription so accounted for only 16.2 percent of the Opioid dollars.

The 10-year utilization trends for the three Opioid cost driver drugs (Exhibit 6) show divergent results, as buprenorphine's share of the Opioid prescriptions increased steadily, climbing from 1.4 percent in 2012 to 5.2 percent in 2021, which coincides with the increased use of MAT plans to treat OUD and buprenorphine's use in combination with naloxone as an antidote to Opioid overdoses. Notably, buprenorphine's share of the Opioid prescriptions hit record levels in 2020 and 2021 after the Drug Enforcement Administration allowed it to be prescribed via telehealth and without an in-person visit in order to allow continued access to care and avoid disruptions in MAT plans during the pandemic. In contrast, oxycodone's share of the Opioid prescriptions was fairly stable between 2012 and 2017 (ranging between 4.9 and 5.4 percent over that six-year span) but increased to 6.0 percent in 2018 and 6.4 percent in 2019 (the first two years following implementation of the formulary and the addition of ACOEM's Chronic Pain and Opioid Guideline into the MTUS) before dropping back to 5.8 percent and 5.9 percent in 2020 and 2021. Meanwhile, tapentadol HCl, used when other pain medications do not work well or cannot be tolerated, ranged between 1.1 and 1.3 percent of the Opioids from 2012 to 2019, but slipped to 0.7 percent in 2020 and 0.6 percent in 2021, less than half of its share a decade earlier.

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

Drug	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Buprenorphine										
% of Opioid Rx	1.4%	1.5%	1.6%	1.7%	2.1%	2.4%	3.1%	4.1%	4.6%	5.2%
Avg Paid	$317	$334	$354	$402	$395	$403	$393	$326	$366	$363
% of Opioid $	4.4%	4.9%	5.4%	6.6%	10.1%	12.4%	15.4%	17.1%	30.2%	35.4%
Oxycodone										
% of Opioid Rx	5.4%	4.9%	5.1%	5.2%	5.1%	4.9%	6.0%	6.4%	5.8%	5.9%
Avg Paid	$409	$358	$376	$326	$279	$255	$225	$207	$176	$146
% of Opioid $	21.7%	17.3%	17.8%	16.3%	17.3%	16.5%	17.1%	16.7%	18.4%	16.0%
Tapentadol HCl										
% of Opioid Rx	1.3%	1.2%	1.2%	1.2%	1.2%	1.1%	1.1%	1.2%	0.7%	0.6%
Avg Paid	$273	$295	$318	$422	$519	$551	$559	$574	$567	$590
% of Opioid $	3.6%	3.5%	3.5%	4.8%	7.8%	7.7%	8.0%	8.4%	7.0%	6.4%

In terms of the payment trends for the three Opioid cost drivers, buprenorphine has seen an eight-fold increase in its share of the Opioid payments as it steadily climbed from 4.4 percent of the Opioid dollars in 2012 to 35.4 percent in 2021. This increase has been driven by the ongoing use of buprenorphine at a time when the use of several other high-cost opioids (*e.g.,* fentanyl, oxymorphone HCl, hydrocodone bitartrate) dropped sharply and/or the average amounts paid for these drugs declined, resulting in a redistribution of payments among the drugs in the Opioid category.

Notably, while buprenorphine's share of the Opioid prescriptions has increased steadily over the past decade, the average amount paid for these prescriptions has fluctuated, increasing from $317 in 2012 to a peak of $403 in 2017, then dropping back to $326 in 2019 before rebounding to $363 in 2021. Much of the decline in the average buprenorphine payments reflects the growing reliance on lower priced generics, which ranged between 8 and 16 percent of the prescriptions dispensed between 2012 and 2016, before increasing to 30 percent in 2017, and to 49 percent in 2018. Since then, generics have ranged between 58 and 63 percent of the buprenorphine prescriptions dispensed to injured workers.

Oxycodone's share of the Opioid payments fell from 21.7 percent in 2012 to 16.5 percent in 2017, as the average payment per prescription fell from $409 to $255. However, since the introduction of the Formulary and the Pain Management and Opioid Guidelines in 2018, oxycodone's share of the Opioid dollars has fluctuated, climbing to 18.4 percent in 2020, then falling to 16.0 percent in 2021, though the average payment has continued to decline, falling to a 10-year low of $146 in 2021. Once again, the impact of generics is evident, as generic versions of oxycodone, which averaged just $23 per prescription in 2021 (versus $106 in 2012) have become much more prevalent in recent years, nearly doubling from 42 percent of the prescriptions in 2012 to 79 percent in 2021. Although they are prescribed far less than they were a decade ago, brand versions of oxycodone still play a key role in maintaining the drug's share of the total Opioid drug spend, as unlike generic versions of the drug, average payments for brand versions of oxycodone have showed little change over the past 10 years, edging down from $630 in 2012 to $615 in 2021. In addition, as with buprenorphine, the declining use of fentanyl and other high-priced Opioids has bolstered oxycodone's position as one of the highest cost opioids still in use in the workers' compensation system.

Changes in tapentadol's share of the opioid drug spend appear more closely tied to the changes in the average payments, as there are no generic versions of this drug. The biggest year-to-year increase in tapentadol's share of the Opioid payments was between 2015 and 2016, when it jumped from 4.8 to 7.8 percent of the Opioid drug spend – an increase that coincided with sharp declines in the share of the Opioid dollars that paid for hydrocodone-acetaminophen (*e.g.*, Vicodin) and fentanyl. From 2012 to 2017, the average payment for tapentadol more than doubled from $273 to $551, then rose to $574 by 2019, after the introduction of the MTUS Formulary and the Pain Management and Opioid Guidelines, before dipping slightly to $567 in 2020, then hitting an all-time high of $590 in 2021.

Tapentadol's share of the total Opioid payments hit a record 8.4 percent in 2019, the combined effect of its 1.2 percent share of the Opioid prescriptions and its average payment of $574, and though the average price hit a new high in 2021, tapentadol's share of the Opioid prescriptions fell to 0.7 percent in

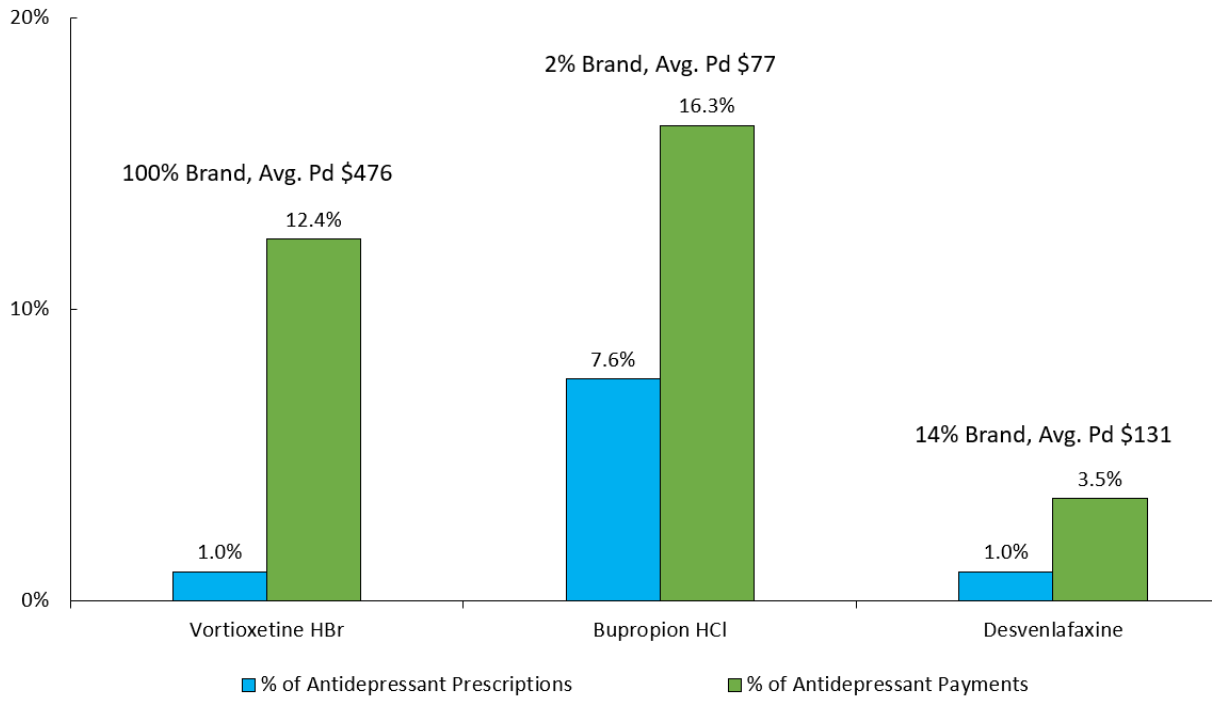
2020 and 0.6 percent in 2021, which offset the impact that the higher average payments had on its share of the total Opioid drug spend.

Antidepressants

Overall, Antidepressants have accounted for an increasing share of California workers' compensation prescriptions over the past decade, and in 2021 they were the fifth most prevalent drug category, representing 7.9 percent of the prescriptions dispensed to injured workers. On the other hand, Antidepressant's share of the workers' compensation overall drug spend last year was just 3.3 percent – down from 5.9 percent a decade earlier, suggesting a shift toward less expensive Antidepressant prescriptions and/or a reduction in the average reimbursements for Antidepressants.

A closer look reveals that the top four Antidepressant medications used in 2021 were all relatively low-cost medications: duloxetine HCl (Cymbalta), trazadone HCl (Desyrel, Oleptro), amitripyline HCl (Elavil), and noripyline HCl (Pamelor), with average payments ranging from $13 to $34 per prescription. Together these four medications, all of which are Exempt drugs in the Formulary, accounted for 64.0 percent of all Antidepressants prescribed in 2021, but because of the low average reimbursements, they consumed just 42.5 percent of the Antidepressant payments. On the flip side, however, the data show three other low-volume, high-cost Antidepressants, vortioxetine HBr (Trintellex), bupropion HCl (Wellbutrin), and desvenlafaxine (Khedezla, Pristiq), all of which are also Exempt drugs, consumed a disproportionate share of the Antidepressant dollars. As shown in Exhibit 7, in 2021 these three medications together accounted for less than 10 percent of the Antidepressant prescriptions dispensed to California injured workers, but 32.2 percent of the Antidepressant drug spend.

Exhibit 7: Percentage of 2021 Antidepressant Prescriptions and Payments



Vortioxetine HBr (Trintellix), is used to treat Major Depressive Disorder in adults by helping restore the balance of serotonin in the brain. Approved by the FDA in 2013 as Brintellix, vortioxetine HBr first appeared in workers' compensation in 2014 when it represented just 0.4 percent of the Antidepressants, but with an average payment $268, it consumed 0.9 percent of the Antidepressant drug spend (Exhibit 8). In 2016, Brintellix was renamed Trintellix to avoid confusion with a similarly named blood clotting drug and that year it increased to 1.2 percent of the workers' compensation Antidepressants, and with the average payment climbing to $350, it jumped to 5.5 percent of the Antidepressant dollars.

Available in 5, 10, and 20 mg tablets, vortioxetine HBr carries a black box warning noting the potential for increased risk of suicidal thoughts and behaviors. Vortioxetine HBr remains under patent, so it is currently only available as brand-name Trintellix. In 2021, claims administrators paid an average of $426 per prescription for this medication, so although it only accounted for 1.0 percent of the Antidepressant prescriptions, it consumed 12.4 percent of the payments within this drug group, ranking third behind duloxetine and bupropion HCl. That percentage, however, was down from 17.7 percent in 2019, when Trintellix accounted for a record 1.6 percent of the Antidepressant prescriptions and the average payment peaked at $450 per prescription.

Exhibit 8: Utilization and Payment 10-Year Growth Trends, Antidepressant Cost Drivers

Drug	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Vortioxetine HBr										
% of Antidepressant Rx	NA	NA	0.4%	0.9%	1.2%	1.1%	1.3%	1.6%	1.4%	1.0%
Avg Paid	NA	NA	$268	$297	$350	$392	$430	$450	$422	$426
% of Antidepressant $	NA	NA	0.9%	2.4%	5.5%	7.2%	11.6%	17.7%	15.3%	12.4%
Bupropion HCl										
% of Antidepressant Rx	10.2%	10.3%	9.6%	8.8%	12.3%	12.2%	10.6%	10.6%	9.0%	7.6%
Avg Paid	$127	$119	$118	$145	$144	$99	$88	$72	$77	$77
% of Antidepressant $	11.5%	9.8%	10.1%	11.7%	22.2%	20.9%	18.7%	19.1%	17.9%	16.3%
Desvenlafaxine										
% of Antidepressant Rx	2.4%	2.4%	2.3%	1.9%	1.9%	1.8%	2.0%	1.9%	1.6%	1.0%
Avg Paid	$176	$220	$264	$314	$367	$257	$137	$115	$150	$131
% of Antidepressant $	3.8%	4.2%	5.5%	5.5%	8.9%	8.0%	5.5%	5.4%	6.2%	3.5%

Bupropion HCl is used to treat a variety of conditions, including depression, anxiety, and other mood disorders, and to aid smoking cessation. In 2021, it accounted for 7.6 percent of the Antidepressants dispensed to California injured workers, but that percentage peaked at 12.3 percent in 2016 and has been in a fairly steady decline ever since. Generic versions of the drug have been available since 2006, and for the past decade generics have increasingly dominated the market, climbing from 96 percent of the bupropion HCl dispensed in workers' compensation in 2012 to 98 percent in 2021.

Brand versions of bupropion, which include extended-release Wellbutrin, tend to be extremely expensive, and while the average reimbursements for generic versions of the drug have declined sharply over the past decade, falling from $121 per prescription in 2012 to $25 in 2021, the opposite has been true for the brand versions, where the average payment per prescription has increased nearly ten-fold from $267 to $2,614. The growing dominance of generic bupropion HCl has helped contain the total amount paid for this medication within the workers' compensation system, as evidenced by the decline in the overall average payment per prescription from the peak level of $145 in 2015 to $77 in 2021. However, the extremely high-cost brand drugs still comprised 2 percent of the bupropion HCl prescriptions in 2021, so the $77 average amount paid for this medication overall was more than three times the $25 average paid for generic versions of the drug, and as a result, bupropion HCl accounted for 7.6 percent of the Antidepressant prescriptions but consumed 16.3 percent of the Antidepressant dollars.

The third low-volume, high-cost Antidepressant identified in the pharmacy data is desvenlafaxine, an extended-release tablet used to treat major depression by adjusting the balance of specific chemicals (serotonin and norepinephrine) in the brain. Available as brand drugs (Pristiq, Khedezla) and as a generic, desvenlafaxine comes in different strengths (25, 50, and 100 mg) and it carries a black box warning due to the potential to worsen depression and increase the risk of suicidal thoughts and actions, especially among people who are 24 years of age or younger. Desvenlafaxine is sometimes used in combination with other medications but interactions with other drugs, vitamins, or herbs can produce harmful side effects, so its use must be closely monitored. The recommended starting dose is 50 mg per day, but prescribers can increase the dosage up to a maximum of 400 mg per day if it is tolerated.

Pristiq was approved by the FDA in 2008 with generic versions approved in 2015 and 2017. It first appeared in California workers' compensation in 2008, when it accounted for 0.5 percent of the antidepressants dispensed that year, but by 2012 that proportion had grown to 2.4 percent and it consumed 3.8 percent of the Antidepressant payments. Prior to the introduction of the generics, desvenlafaxine's share of the workers' compensation Antidepressants peaked at 2.5 percent in 2011 and over the following decade it gradually declined to just 1.0 percent of the prescriptions within its drug group.

Brand-name Pristiq dominated the market through 2016, with generic versions of the drug accounting for just 1 percent of the desvenlafaxine dispensed to injured workers that year, but with the approval of more generics that proportion grew to 70.0 percent in 2017, and in 2018 the generic's share increased to 90 percent of the prescriptions for this drug. In the three subsequent years brand versions of the drug ranged between 14 percent and 15 percent of the prescriptions, with average payments for the brand versions climbing as high as $642 per prescription compared to $58 to $66 for the generics.

Though the brand version of desvenlafaxine continues to represent a relatively small share of the prescriptions, the high amounts paid for those prescriptions have driven the overall average reimbursement for the drug upward, with overall payments ranging between $115 and $150 since 2019. Thus, in 2021, desvenlafaxine represented just 1.0 percent of the Antidepressant prescriptions, but 3.5 percent of the Antidepressant drug spend.

Summary

This second report in the Institute's research series highlighted nine drugs within the Dermatological, Opioid, and Antidepressant categories that have a disproportionate impact on the total cost of medications within their drug groups relative to their share of the prescriptions and discussed factors that influenced the amounts paid for these drugs over the 10-year study period.

The 10-year trend data for the drugs highlighted in the series also confirm that while Opioid use has been in a steady decline, and physicians have diligently attempted to find alternative painkillers, doing so has been an ongoing challenge. The shifts in the mix of drugs used in workers' compensation make it clear that the 2013 introduction of the Independent Medical Review process to resolve disputes over pharmaceutical and other medical service requests had a direct impact on the types of drugs used to treat injured workers, as did the adoption of the Pain Management and Opioid Guidelines into the MTUS in late 2017 and the implementation of the MTUS Prescription Drug Formulary in January 2018.

Many of the drugs reviewed in this series receive little attention because they account for a relatively small share of the prescriptions dispensed to injured workers, though the high average amounts paid for these drugs make them significant cost drivers. For example, in 2021, the three Dermatological drugs noted in this report together accounted for just 3.0 percent of the prescriptions in their therapeutic drug group, but they consumed 19.3 percent of the Dermatological dollars. Similarly, the three Opioids represented 11.7 percent of the prescriptions in their drug group, but 57.8 percent of the payments; and the three Antidepressants accounted for 9.6 percent of the prescriptions in their group, but 32.2 percent of total Antidepressant reimbursements.

As noted in Part I of this research series, the total amount paid for medications within a therapeutic drug group can reflect several factors besides the volume of prescriptions, including the fees that are allowed for the various drugs by the Pharmacy Fee Schedule, the average quantities and dosages dispensed, the mode of delivery, and the availability of generics or over-the-counter versions of the drug. In cases such as the Opioid tapentadol HCl or the Antidepressant vortioxetine HBr, the medication may be a single-source, brand drug with no generic alternatives, so until the patent expires, the manufacturer has a monopoly on the medication. In some cases, manufacturers have also received FDA approvals for reformulated versions of the drug (*e.g.*, an extended-release or abuse-deterrent version, or a new dosage) which has allowed them to extend their patent and maintain control over pricing. In other cases, such as the Opioid buprenorphine, which is often used to treat Opioid Use Disorder, a wide variety of generic and brand formulations are available, but with huge price differentials that can drive up the average amount paid for the drug. For example, in 2021 the average payment for generic buprenorphine was $195 versus $594 for brand versions, while average payments for buprenorphine administered via patch or film ranged from a few hundred dollars to well over $1,000 per prescription, so even though 58 percent of the buprenorphine prescriptions were generics, the overall average payment was $363 per prescription, or 86.2 percent higher than the $195 average paid for a generic.

Other types of medications also bear careful consideration, as evidenced by the Dermatological drugs highlighted in this report. In some cases, there may be confusion over prescriptions for medications that

contain the same or similar active ingredients. For example, with the decline in the use of Opioids, use of moderately priced generic versions of diclofenac sodium (average payment, $60) has become widespread, but brand-name versions that average more than $600 per prescription are still available and are sometimes dispensed. At the same time, Xrylix, the private-label kit containing a diclofenac solution and adhesive sheets, also continues to be dispensed by a handful of pharmacies, but because it is not listed in the Medicaid database and has no FUL, claims administrators pay 83 percent of the AWP, which in 2021 led to average payments of $4,126 per prescription. As a result, Xrylix, which represented only 0.3 percent of Dermatological prescriptions dispensed in 2021, accounted for 7.2 percent of the total Dermatological drug spend within the workers' compensation system.

Similarly, lidocaine/menthol medications come in many different forms, including brand and generic versions, as well as over-the-counter products. Though many are inexpensive, and single-ingredient lidocaine patches are in the MTUS Formulary and were recently reclassified as an Exempt drug, the data show that the two high-priced, private-label lidocaine/menthol prescriptions, NuLido gel (average 2021 payment of $422) and Terocin patches (average payment of more than $1,000 for 30 patches), have become key Dermatological cost drivers, even though neither is listed in the Formulary. The payment data reveal that while some NuLido and Terocin prescriptions are physician dispensed, most are dispensed by smaller pharmacies or by mail order, though as "Not Listed" drugs, they are subject to prospective UR, and it is incumbent on the prescriber to show that their use is supported by the MTUS or other guidelines.

While the selection of a high-cost medication to cure or relieve an injured worker's specific condition may be entirely appropriate, both providers and payers need to ensure that such choices are based on solid clinical judgment supported by evidence-based medicine, as well as a full understanding of the available alternatives. Part of that responsibility – especially in the case of Opioids and the Antidepressants highlighted in this report – includes careful consideration of the risks, including potential drug interactions and long-term repercussions, as well as the need for patient monitoring and assessment. For example, much of the buprenorphine that is now used in workers' compensation is prescribed as part of a MAT plan to try and wean injured workers with legacy claims off of other more potentially dangerous Opioids that were initially prescribed to treat chronic pain, but which can become less effective as the patient builds up a tolerance to the drug.

Institute research on low-volume/high-cost medications will continue with Part III in the series, which will focus on medications found in the Musculoskeletal and Ulcer drug categories. In the meantime, CWCI members who would like more detail on California workers' compensation prescription drug utilization and reimbursement can log on to our website (www.cwci.org) and click Interactive Research Tools under the Research tab to access CWCI's Prescription Data Application as well as the MTUS Formulary Interactive Tool which has prescription data broken out by MTUS Formulary category.

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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 76% 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).

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