California Workers' Compensation Institute

Spotlight Report

Emerging Drug Classes in California Workers' Compensation: Psychotherapeutic & Neurological Drugs

Bob Young **February 2026**

Background

In 2023, a three-part CWCI research series identified 23 low-volume, high-priced drugs in seven therapeutic drug groups that had become cost drivers within their groups and explored factors that fueled the growth in the average payments for those drugs. Part I of the series focused on Anti-Inflammatories and Anticonvulsants,[1] which ranked first and second in terms of California workers' compensation prescription volume in 2022; Part II focused on Opioids, Dermatologicals and Antidepressants,[2] which ranked third, fourth, and fifth; and Part III focused on Musculoskeletal and Ulcer Drugs,[3] which were the sixth and seventh most heavily prescribed drug groups.

Those studies used data from CWCI's Prescription Drug Interactive Application, which at the time included records on prescriptions dispensed to injured workers from January 2010 through December 2022. Since then, ongoing updates to the application have generated additional data on California workers' compensation prescriptions dispensed through June 2025, so the application now encompasses 6.5 million prescriptions and more than $687 million in payments. In reviewing the latest results, it became evident that Psychotherapeutic & Neurological Drugs, though still representing only a very marginal share (0.3 percent) of all prescriptions dispensed to California injured workers in 2024, are emerging as a prescription drug cost driver, as their share of the total drug spend within the system has increased nearly fivefold over the past decade, climbing from 0.7 percent in 2015 to 3.4 percent in 2024.

To explore what is behind the growth in payments for these drugs, CWCI undertook this study to examine how and when various Psychotherapeutic & Neurological Drugs are used to treat injured workers, changes in the average amounts paid for these prescriptions, and changes in the mix of Psychotherapeutic & Neurological drugs used to treat California injured workers over the past decade.

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[1] 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, February 2023.
[2] 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.
[3] Young, B., Jones, S. *Cost-Driver Medications in the Top California Workers' Comp Therapeutic Drug Groups, Part III: Musculoskeletal and Ulcer Drugs*. CWCI Spotlight Report, July 2023.

CWCI's Industry Research Information System (IRIS) database[4] monitors 31 different Psychotherapeutic & Neurological Drugs, but most of them were dispensed in very low volume during the 10-year study period and many of them had little impact on the total amount paid for medications in this drug group. Therefore, this report focuses on five of the most commonly prescribed drugs that at various points over the past decade have accounted for a significant share of the Psychotherapeutic & Neurological Drug prescriptions and/or drug spend: memantine HCl (Namenda); donepezil hydrochloride (Donepezil HCl); extended-release gabapentin enacarbil (Horizant ER); once-daily gabapentin (Gralise); and dextromethorphan hydrobromide quinidine sulfate (Nuedexta).

Together, these five drugs comprised 92.9 percent of the Psychotherapeutic & Neurological Drugs dispensed to California injured workers in 2024, and 59.7 percent of the drug spend for this drug group.

Psychotherapeutic & Neurological Drugs

Psychotherapeutic Drugs modify mood and behavior by altering the activity or levels of brain chemicals (neurotransmitters) such as serotonin, dopamine, norepinephrine, and gamma-aminobutyric acid (GABA). Neurological Drugs, on the other hand, target various aspects of the nervous system and are used to treat conditions including seizures, nerve pain, and neurodegenerative diseases like dementia.[5] The brain is the central organ of the nervous system, so drugs that affect neurological pathways often have psychotherapeutic effects, while Psychotherapeutic Drugs interact with receptors in the nervous system and can produce changes in physiological or psychological functions. Psychotherapeutic & Neurological Drugs are prescribed for several specific conditions including shingles-related pain, restless leg syndrome and other movement disorders, narcolepsy, dementia, and pseudobulbar affect, or PBA, which is described as "emotional incontinence" marked by uncontrollable and inappropriate laughter and/or crying that doesn't match how the individual is feeling.[6]

Detailed IRIS data on the drugs in this group show that in California workers' compensation they have been used to treat injured workers with head, cranial, and intracranial injuries that result in concussions, fractures, lacerations, or multiple physical and psychological injuries, as well as diseases and disorders of the spine or joints, and movement disorders. The market for these drugs has evolved over the past decade and the mix of drugs used in workers' compensation has shifted, but all five drugs highlighted in this report were dispensed to injured workers in 2024 and in most, if not all, of the 10-year study period, which included the first seven years following implementation of the Medical Treatment Utilization Schedule (MTUS) Prescription Drug Formulary.[7]

[4] IRIS is CWCI's proprietary database. Version 2025Q2, used for the latest version of the Prescription Drug App, contains data on employee and employer characteristics, medical service data, benefits, and administrative costs on about 10 million California workers' comp claims from AY 2000 – Q2 2025, valued through June 2025.
[5] MedlinePlus. Antidepressants and Other Psychiatric Medications; and Drug Information for Neurologic Conditions, U.S. National Library of Medicine, 2025.
[6] De Faria Sousa, B. and Espinosa, J. PBA: A Network Disorder Linking Emotion, Neurobiology, and Therapeutics, Cureus. 2025
[7] In 2015 Gov. Brown signed AB 1124 which mandated that the DWC create an evidence-based Workers' Compensation Prescription Drug Formulary and called for the Formulary to be incorporated into the Medical Treatment Utilization Schedule. The Formulary was adopted in 2017 and took effect January 1, 2018.

Data and Methods

CWCI's Prescription Drug Interactive Application contains detailed data on California workers' compensation prescriptions extracted from our IRIS database. Each drug is identified by its National Drug Code (NDC) and descriptive data from Medi-Span,[8] including its therapeutic drug group, active ingredient name, and availability as a brand or generic drug. The December 2025 version of the application has data on 6.5 million prescriptions dispensed between January 2013 and June 2025, with aggregate payments for those drugs totaling more than $687 million.

The service year detail in the application (based on the fill date for each prescription) ranks therapeutic drug groups by prescription volume and total reimbursements, and notes the average amounts paid per prescription and the percentage of the prescriptions dispensed as brand and generic drugs. Results can be displayed for an entire drug group or for specific medications in the group. For this report, the author used Prescription Drug Interactive Application data on Psychotherapeutic & Neurological Drugs dispensed on medical-only and indemnity claims between January 2015 and the end of 2024 (the last full year for which data was available) to rank the drugs based on their percentage of the prescriptions and total payments within the group. The 10-year prescription and payment trends shown in Exhibit 1 are also based on those service year 2015 through 2024 prescriptions.

The California workers' compensation pharmaceutical market constantly changes as new drugs are introduced, older drugs are retired or reformulated (e.g., an extended-release version may be introduced or the mix of ingredients may be altered), patents on brand drugs expire and generics enter the market, and revisions are made to the treatment guidelines and the MTUS Formulary. To assure that the data is robust enough to provide valid measurements, CWCI's Prescription Drug Interactive Application only includes drugs with payment records for at least 30 prescriptions dispensed within a given year. In the case of the 31 Psychotherapeutic & Neurological Drugs monitored by the IRIS database during the 10-year study period, most were not dispensed in significant volume, though in several cases the average amounts paid were quite high compared to the average for this drug group.[9] That left only eight Psychotherapeutic & Neurological Drugs that represented both a significant share of the prescriptions and a significant share of the total dollars paid in the drug group within the study period.

This analysis focuses on five drugs in the group that were dispensed in 2024 and throughout most, if not all, of in the 10-year study period, and uses service year detail from the Prescription Drug Interactive Application to track changes in each drug's share of the prescriptions and payments, as well as the average amounts paid per prescription. Two of the drugs were primarily dispensed as generics throughout the study period and were relatively inexpensive as a result; two were dispensed only as brand drugs; and one was dispensed as a brand drug until a generic became available in 2024.

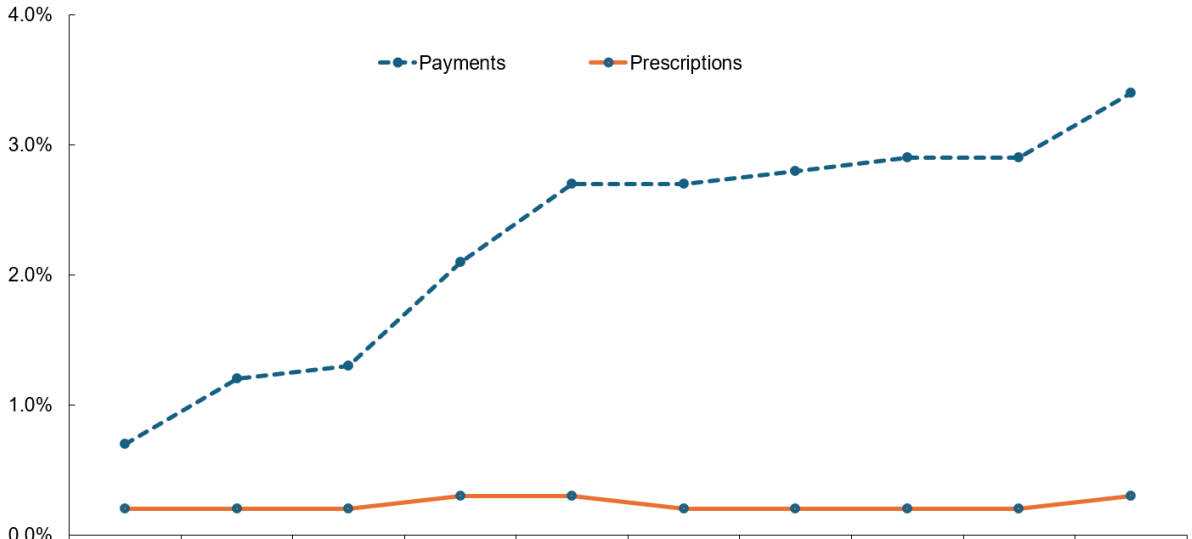
[8] Master Drug Data Base (MDDB) Version 2.5 Documentation Manual, Wolters Kluwer Health, Medi-Span.
[9] Two prime examples of very low volume/very high-cost drugs in this group are Sodium Oxybate (Xyrem and Lumryz), used to treat narcolepsy, for which the average reimbursement per prescription in 2024 was $18,513, and Valbenazine Tosylate (Ingrezza), used for Tardive Dyskenesia and other movement disorders, which had an average payment of $7,481 per prescription in 2024.

In addition to the pricing and payment data, the author used prescription detail from the IRIS database to confirm where the drugs were dispensed; the manufacturer; and the formulation, quantity, dosage, and brand dispensed. The Results section of this report includes background information on each of the five drugs and tracks their utilization and reimbursement, noting each drug's share of the prescriptions within the Psychotherapeutic & Neurological Drug group for service years 2015 through 2024, the percentage of the drug spend that each medication represented within the drug group across that 10-year span, and the change in the average amount paid per prescription over that decade.

Results

Psychotherapeutic & Neurological Drugs have consistently accounted for just a tiny fraction of all prescriptions dispensed to California injured workers, ranging between 0.2 percent and 0.3 percent of all workers' compensation prescriptions dispensed from 2015 through 2024 (Exhibit 1), even while other drug groups—most notably Anti-Inflammatories and Anticonvulsants—saw their share of the prescriptions increase sharply as the use of Opioids plummeted.[10] The Psychotherapeutic & Neurological Drugs' marginal share of the prescriptions throughout the decade reflects the fact that these are specialty drugs used in a small number of claims involving unique risks, though in some cases they appear to have been prescribed for off-label treatment of common work injuries.

Exhibit 1. Psychotherapeutic & Neurological Drugs as a Percent of Calif WC Prescriptions & Drug Spend, 2015-2024



	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
Payments	0.7%	1.2%	1.3%	2.1%	2.7%	2.7%	2.8%	2.9%	2.9%	3.4%
Prescriptions	0.2%	0.2%	0.2%	0.3%	0.3%	0.2%	0.2%	0.2%	0.2%	0.3%

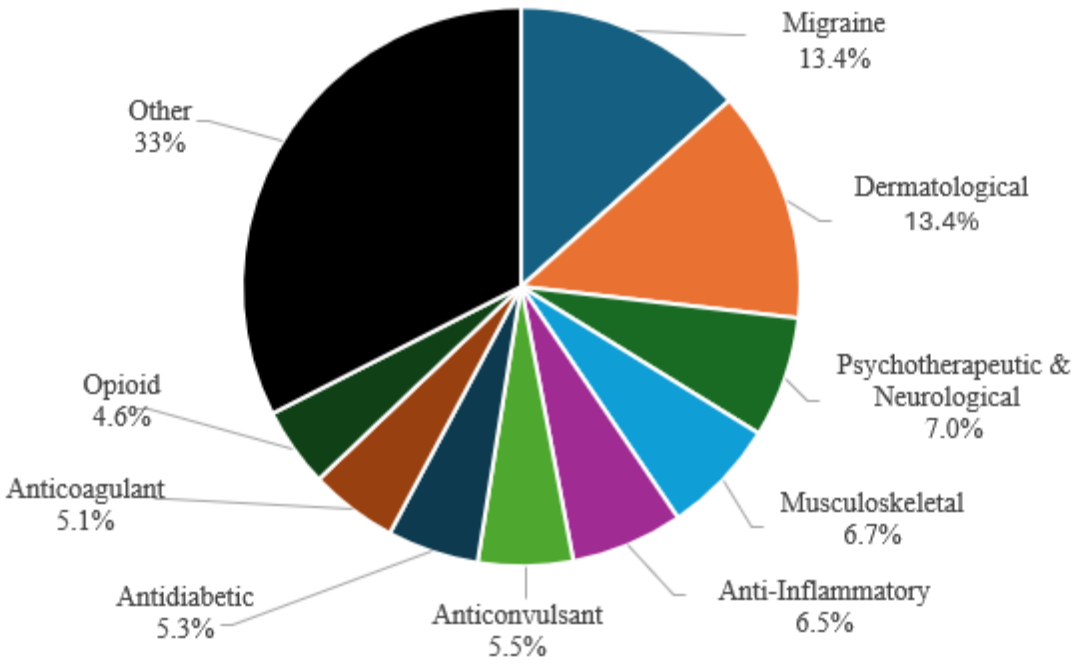
While utilization of Psychotherapeutic & Neurological Drugs was limited throughout the 10-year study period, their share of the total drug spend was consistently higher than their share of the prescriptions due to the high cost of several of the drugs, and that gap widened as Psychotherapeutic & Neurological

[10] Young, B., Secia, J., Hayes, S. *California Workers' Comp Prescription Drug Trends*, CWCI Research Update, Mar 2021.

Drugs' share of the total drug spend increased sharply. Exhibit 1 shows that even though this drug group's share of workers' compensation prescriptions was stable, its share of the total drug spend rose nearly fivefold from 0.7 percent in 2015 to 3.4 percent in 2024, with no declines noted during that 10-year span.

Data on the average payment per prescription over the past decade underscore the reason for the growth in this group's share of the prescription dollars, as the average payment for drugs in the group increased from $409 in 2015 to $1,147 in 2024, with much of that growth due to the use of high-cost brand drugs, where average payments in this drug group more than quadrupled from $451 in 2015 to $1,955 in 2024. As a result, payments for brand name Psychotherapeutic & Neurological Drugs jumped from 1.8 percent of all California workers' compensation brand drug payments in 2015 to 7.0 percent in 2024 (Exhibit 2), ranking third among all drug groups behind Migraine Drugs and Dermatological Drugs , but ahead of Musculoskeletals, Anti-Inflammatories, Anticonvulsants, Antidiabetics, Anticoagulants, and Opioids.

Exhibit 2. Distribution of California Workers' Compensation Brand Name Drug Payments by Drug Group Service Year 2024



Distribution of Psychotherapeutic & Neurological Drug Claims by Diagnosis

To identify the types of work injury claims associated with Psychotherapeutic & Neurological Drug use, the Institute examined detailed IRIS data on claims in which these drugs were dispensed, noting the ICD-10 codes for the claims and assigning each to a primary diagnostic category using a proprietary grouping system (DxCat). The resulting distribution of Psychotherapeutic & Neurological Drug claims by diagnosis was then compared to the distribution for claims in which other drugs were dispensed.

Exhibit 3 shows Psychotherapeutic & Neurological Drug claims were more heavily concentrated among their top diagnostic categories, as the top 10 categories accounted for 92.7 percent of the Psychotherapeutic & Neurological Drug claims while the top 10 categories for claims involving other drugs accounted for 82.5 percent of those claims. The top diagnostic category for Psychotherapeutic & Neurological Drug claims was diseases and disorders of the spine, which represented 44.0 percent of the claims—about 2-1/2 times the percentage noted for claims involving other drugs, while more than a quarter of the Psychotherapeutic & Neurological Drug claims involved head, cranial, and intracranial injuries, a category that was not among the top 10 diagnoses for claims involving other drugs.

Exhibit 3. Top Diagnoses, Psychotherapeutic & Neurological Drug Claims v. Other Drug Claims

	Claims w/Psychotherapeutic & Neurological Drugs	Pcnt		Claims w/Other Drugs	Pcnt
1	Diseases/disorders – spine	44.0%		Strains/sprains/dysfunctions – non-vert	17.1%
2	Injury – head, cranial, intracranial	25.8%		Diseases/disorders – spine	16.6%
3	Diseases/disorders – joints	5.6%		Strains/sprains/dysfunctions – spine	11.6%
4	Trauma - diseases/disorders – joints	4.0%		Superficial injury	8.3%
5	Fracture – lower extremities	2.9%		Disorders – connective, soft tissue, bone	5.8%
6	Diseases – nervous system	2.9%		Trauma – diseases/disorders – joints	5.4%
7	Crushing injury or traumatic amputation	2.4%		Wounds – finger, thumb, toe	5.2%
8	Disorders – connective, soft tissue, bone	1.9%		Diseases/disorders – joints	5.2%
9	Fracture – spine or pelvis	1.9%		Open wounds – 2nd, 3rd degree burns	4.7%
10	Fracture – shoulder, arm	1.3%		Diseases and injury of the eye	2.6%
	Subtotal:	92.7%			82.5%

Joint diseases and disorders were the third most common diagnostic category for the Psychotherapeutic & Neurological Drug claims (5.6 percent)—but that percentage was about the same as the 5.2 percent share noted for claims with other drugs. Trauma due to joint diseases and disorders represented a slightly smaller share of Psychotherapeutic & Neurological Drug claims than claims with other drugs (4.0 percent vs. 5.4 percent), while connective tissue, soft tissue, and bone disorders were 3 times more prevalent among the claims with other drugs (1.9 percent vs. 5.8 percent).

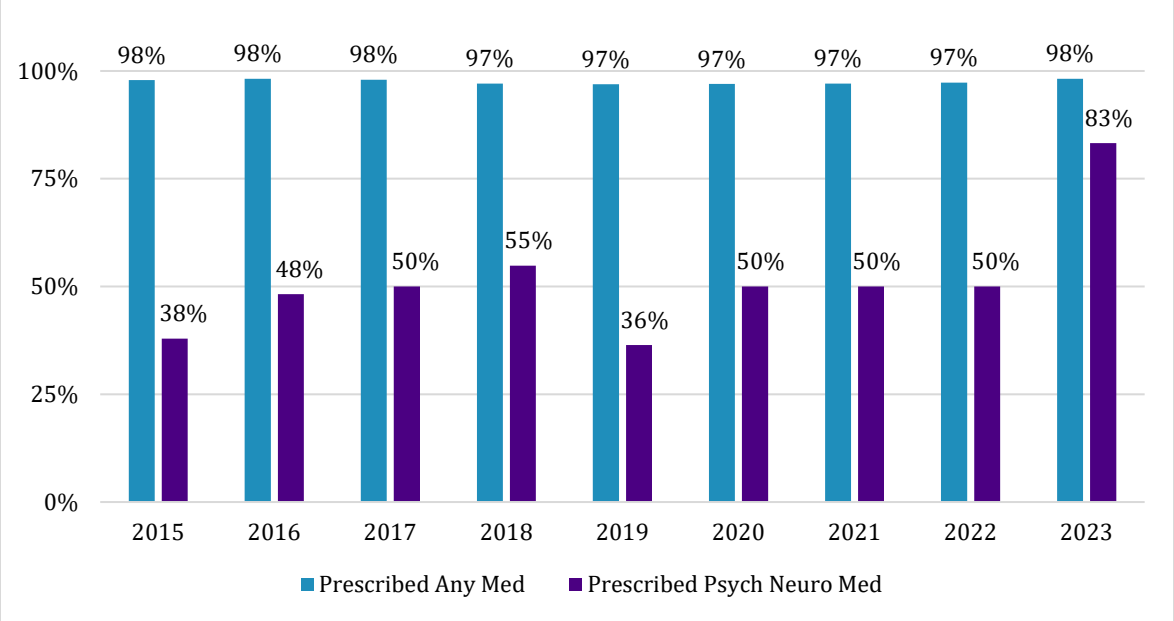
Diagnostic categories on the top 10 list for Psychotherapeutic & Neurological Drug claims that were not on the top 10 list for claims with other drugs included the aforementioned head, cranial, and intracranial injuries (25.8 percent); lower extremity fractures (2.9 percent); nervous system diseases (2.9 percent); crushing injuries or traumatic amputations (2.4 percent), spine or pelvis fractures (1.9 percent), and shoulder and arm fractures (1.3 percent). Conversely, the top 10 diagnostic categories for claims with other drugs included six diagnoses groups that were not among the top 10 for the Psychotherapeutic & Neurological Drug Claims: non-vertebrae strains, sprains and dysfunctions (17.1 percent); strains, sprains and dysfunctions of the spine (11.6 percent); superficial injuries (8.3 percent); finger, thumb and toe wounds (5.2 percent); open wounds – second and third degree burns (4.7 percent); and eye diseases and injuries (2.6 percent). Several of the top diagnostic categories for the claims with other drugs included more minor injuries than those associated with Psychotherapeutic & Neurological Drug claims.

Recent Utilization, Reimbursement and Timing of Psychotherapeutic & Neurological Drugs

With only 0.3 percent of all California workers' compensation prescriptions dispensed in 2024 Psychotherapeutic & Neurological Drugs ranked 28th out of 88 therapeutic drug groups in terms of utilization, but their 3.4 percent share of workers' compensation pharmaceutical payments made them the number 9 drug group in terms of the total 2024 drug spend. That put them just behind Antidepressants, which consumed 4.4 percent of all 2024 prescription dollars, and Opioids, which consumed 4.3 percent, though both those drug groups were dispensed in much higher volumes, as Antidepressants represented 7.7 percent of the 2024 prescriptions and Opioids represented 6.9 percent.

To examine when Psychotherapeutic & Neurological Drugs are first dispensed the author used AY 2015 to AY 2023 claims data and compared the initial treatment date on the claim to the first prescription fill date. Comparing results for Psychotherapeutic & Neurological Drug claims to claims with any medications showed Psychotherapeutic & Neurological Drugs were much less likely to be dispensed in the first year of treatment. Exhibit 4 shows that between AY 2015 and AY 2023, 97 to 98 percent of claims that had any type of drug prescribed had at least one prescription filled in the first year of treatment. In contrast, the percentage of Psychotherapeutic & Neurological Drug claims that had a drug within that group dispensed in the first year ranged between 36 and 83 percent, indicating that these drugs were more likely to be dispensed later in the life of the claim. Notably, the relatively high percentage of 2023 claims with Psychotherapeutic & Neurological Drugs dispensed in the first 12 months is due in part to the fact that these were newer claims that had a shorter amount of time beyond the first year of treatment in which the drugs could have been dispensed. As the AY 2023 claims age and more of them have Psychotherapeutic & Neurological Drugs prescribed at some point beyond the first year of treatment, the percentage of claims that had these drugs prescribed in the first year will decline.

Exhibit 4. Percent of AY 2015- 2023 Claims Prescribed Medication w/in 1st Year of Treatment

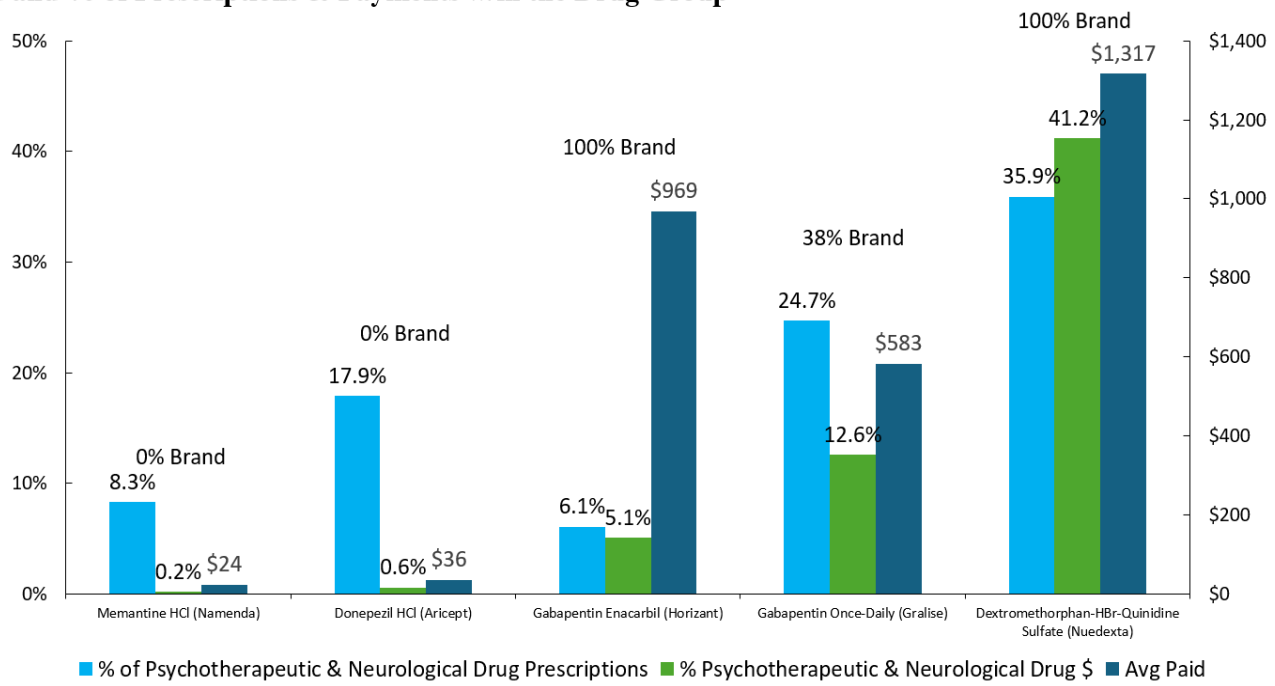


Overall, less than half (47 percent) of the AY 2015-2023 claims with Psychotherapeutic & Neurological Drug prescriptions had a medication from that drug group dispensed in the first year of treatment, while 98 percent of claims involving any medications had an initial fill date in the first year. The AY 2016 to AY 2022 claims data showed a fairly consistent pattern in which about half of all Psychotherapeutic & Neurological Drug claims had the initial prescription dispensed in the first year of treatment. The only exception was AY 2019 when the rate fell to 36 percent, and for many of the AY 2019 claims the first year of treatment would have included the initial months of the pandemic which was declared in March 2020.

The Top 5 Psychotherapeutic & Neurological Drugs

Since 2019, only five Psychotherapeutic & Neurological medications have been dispensed in sufficient volume to be included in CWCI's interactive application. Those five drugs are noted in Exhibit 5, along with their share of the 2024 prescriptions and payments within the drug group, the average amount paid, and the percentage that were dispensed as brand drugs.

Exhibit 5. Top 5 Calif WC Psychotherapeutic & Neurological Drug Prescriptions, 2024 Fill Dates Avg. Paid and % of Prescriptions & Payments w/in the Drug Group



One of those five drugs (immediate release memantine hydrochloride, brand name Namenda), was initially approved by the FDA in 2003 to treat Alzheimer's disease and dementia,[11] but it is also used to prevent neurocognitive decline after whole brain radiotherapy.

[11] Drug Approval Package: Namenda HCl Tables (Memantine). U.S. Food & Drug Administration, Oct. 16, 2003.

The FDA approved an extended-release version of Namenda in 2010,[12] and in 2014 it approved memantine and another Psychotherapeutic & Neurological Drug, donepezil, as a combination drug (Namzaric) to treat Alzheimer's.[13] At that point, memantine HCl was still only available as a brand drug.

As shown in Exhibit 6, in 2015, memantine HCl accounted for 7.4 percent of the Psychotherapeutic & Neurological Drugs dispensed to California injured workers, and with an average payment of $309 it consumed 5.6 percent of the total drug spend for its drug group. By mid-2015, however, after receiving FDA approvals, Mylan and Dr. Reddy's Laboratories introduced generic versions of memantine HCl,[14,15] and both the utilization and the average amount paid for the drug began to decline.

In 2018, 2021, 2022, and 2023, the number of memantine prescriptions in the IRIS database was so low that the volume was insufficient to be included in CWCI's Interactive Pharmacy App, though it did increase in 2024, when it accounted for 8.3 percent of the Psychotherapeutic & Neurological Drug prescriptions.

Exhibit 6: 2015–2024 Calif WC Utilization & Payment Trends, Memantine HCl

	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
Memantine HCl (Namenda)										
% of Psychotherapeutic & Neurological Drug Rx	7.4%	3.8%	2.6%	NA	3.4%	5.8%	NA	NA	NA	8.3%
Avg Paid per Rx	$309	$188	$258	NA	$175	$137	NA	NA	NA	$24
% of Psychotherapeutic & Neurological Drug Spend	5.6%	1.3%	1.3%	NA	0.7%	0.8%	NA	NA	NA	0.2%

Since it was implemented in January 2018, the MTUS Prescription Drug Formulary has categorized memantine HCl as a Non-Exempt drug, so it has been subject to prospective utilization review (UR) for the past seven years. Even before that, however, it was used sparingly, representing between 2.6 percent and 7.4 percent of the Psychotherapeutic & Neurological Drug prescriptions dispensed between 2015

[12] FDA Approves NAMENDA XR for the Treatment of Moderate to Severe Dementia. Pharmaceutical Processing, June 22. 2010.
[13] Actavis and Adamas Announce FDA Approval of Namzaric for Alzheimer's Disease. Pharmaceutical Processing, Dec. 24, 2014.
[14] "Mylan One of First to Launch Generic Version of Namenda Tablets." PR Newswire, Mylan N.V., July 14, 2015.
[15] Alzheimer Generic Launched in the U.S. Generics and Biosimilars Initiative News Release. Aug. 28, 2015.

and 2017. With generic versions available the average payment has continued to decline, most notably in 2024 when the average fell to $24 per prescription, so it has not been a significant cost driver.

Likewise, donepezil hydrochloride, (brand name Aricept), which is sometimes used in combination with memantine HCl for Alzheimer's patients, has not been a significant Psychotherapeutic and Neurological cost driver, even though its share of the prescriptions within that drug group nearly doubled over the past decade from 9.2 percent in 2015 to 17.9 percent in 2024 (Exhibit 7).

Exhibit 7: 2015–2024 Calif WC Utilization & Payment Trends, Donepezil HCl

	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
Donepezil Hydrochloride (Aricept)										
% of Psychotherapeutic & Neurological Drug Rx	9.2%	7.3%	8.3%	10.6%	12.0%	10.6%	13.6%	11.9%	15.0%	17.9%
Avg Paid per Rx	$104	$41	$61	$44	$11	$11	$25	$46	$38	$36
% of Psychotherapeutic & Neurological Drug Spend	2.3%	0.6%	0.9%	0.6%	0.1%	0.1%	0.3%	0.5%	0.5%	0.6%

First approved for use by Alzheimer's patients in the U.S. in 1996, donepezil HCl has also been studied for conditions such as mild cognitive impairment and post-coronary artery bypass surgery cognitive impairment, which could result from work-related injuries. Although the Food and Drug Administration (FDA) has not approved the drug for these conditions, doctors have often prescribed it off-label,[16] so it may have been prescribed to injured workers for such purposes. The FDA approved a generic version of the drug in 2010,[17] and while the average payment per prescription was $104 in 2015, the availability of generic versions over the past decade has significantly reduced the cost. Since 2016 the average workers' compensation payment has ranged between $11 and $61 per prescription, and since 2019 it has fluctuated between $11 and $46. As a result, over the past six years donepezil HCl has never represented more than 0.6 percent of the payments in its drug group even as its share of the Psychotherapeutic & Neurological prescriptions hit a record 17.9 percent in 2024.

One factor that may have spurred the recent growth in donepezil HCl's share of Psychotherapeutic & Neurological prescriptions is its classification within the MTUS Formulary. From the time the Formulary initially took effect in January 2018 until February 15, 2019, donepezil HCl was an Unlisted

[16] UCLAhealth.org, "Alzheimer's Drug Prescribed 'off label' for mild cognitive impairment could pose risk for some," UCLA Research Alert, Feb. 23, 2017
[17] "FDA Approves Generic Aricept," U.S. Pharmacist, Feb. 19, 2010.

drug, which could be prescribed as long as the treating physician could show how its use was supported by the MTUS or other applicable treatment guidelines for the condition or injury being treated. In February 2019, the state adopted Version 4 of the Formulary, and donepezil HCl was recategorized as an Exempt drug[18] so it could be dispensed without prospective UR. After it was recategorized as an Exempt drug, donepezil HCl's share of the Psychotherapeutic & Neurological Drugs jumped from 11.6 percent in 2018 to 17.2 percent by 2024, though as noted, with low-cost generics widely available, the average payment did decline, and while its share of the payments within its drug group has increased over the past six years, it has not exceeded 0.6 percent.

Unlike memantine HCl and donepezil HCl, two of the other Psychotherapeutic & Neurological Drugs highlighted in this report—gabapentin enacarbil ER (Horizant) and dextromethorphan HBr quinidine sulfate (Nuedexta)—were only available as brand drugs during the entire 10-year study period, while the third drug, once-daily gabapentin (Gralise) was not released as a generic until the end of the study period in early 2024. The lack of generic alternatives kept the payments for these drugs relatively high compared to memantine HCl and donepezil HCl. That payment disparity continued in 2024. As noted previously, the average amounts paid for memantine HCl and donepezil HCl prescriptions in 2024 were $24 and $36 respectively, while CWCI's Prescription Drug Application shows reimbursements averaged $583 for once-daily gabapentin; $969 for gabapentin enacarbil (ER), and $1,317 for dextromethorphan HBr quinidine sulfate.

Once-daily gabapentin and dextromethorphan HBr quinidine sulfate were the most heavily prescribed medications in this drug group in 2024, together accounting for 60.6 percent of the Psychotherapeutic & Neurological Drugs prescriptions dispensed and 53.8 percent of the total payments for this drug group, with gabapentin enacarbil (ER) representing 6.1 percent of the prescriptions and 5.1 percent of the Psychotherapeutic & Neurological Drug payments.

The high average payments for these three drugs, combined with their share of the prescriptions, have made them among the most significant Psychotherapeutic & Neurological Drug cost drivers over the past decade, so the following sections take a closer look at each of these drugs and their utilization and payment trends within the California workers' compensation system.

Gabapentin Enacarbil (Horizant)

The Anticonvulsant gabapentin has been around for more than 30 years and was the third most heavily used medication in California workers' compensation in 2024, accounting for 6.2 percent of all prescriptions dispensed to injured workers and 1.9 percent of the total drug spend. Prior Institute research documented a significant increase in the use of gabapentin as a pain reliever as Opioids fell out

[18] In January 2019, the DWC announced updates to the MTUS Drug List, adopting and incorporating by reference drugs addressed in ACOEM's Traumatic Brain Injury (TBI) Guideline. These included Donepezil HCl, which was added as an exempt drug, and Dextromethorphan HBr Quinidine Sulfate (Nuedexta), which was added as a non-exempt drug, (subject to prospective UR) in V.4 of the Drug List, which took effect 2/15/19. The drug list reference to the ACOEM Guideline noted Donepezil HCl was recommended for TBI, but there was no recommendation on the use of Nuedexta for TBI. DWC Posts Updated MTUS Drug List Effective February 15 | California Department of Industrial Relations.

of favor over the past dozen years,[19] but when gabapentin dosages are increased less of the drug is absorbed, which limits its use for the treatment of some conditions.

To address the issue, gabapentin enacarbil, which uses high-capacity nutrient transporters in the intestines to allow more predictable and extended absorption of gabapentin, was developed in the 1990s, allowing for once or twice a day dosing.[20] After several years of clinical trials and an initial rejection by the FDA due to inadequate safety data, in April 2011 gabapentin enacarbil was approved as a Neurological Drug for restless leg syndrome,[21] though the FDA cautioned that use of this drug can result in dizziness, drowsiness, loss of coordination, and driving impairment. The drug also received subsequent approval in June 2012 for postherpetic neuralgia (PHN) – nerve pain resulting from shingles.[22] Other than these two uses, gabapentin enacarbil (ER) has not been approved by the FDA as a treatment for other conditions, and it is not interchangeable with gabapentin as the two drugs have been approved as treatments for different ailments.

Gabapentin Enacarbil ER first appeared in the IRIS data in 2015, three years after it was approved for PHN, when it represented 8.1 percent of the Psychotherapeutic & Neurological Drug prescriptions dispensed to California injured workers (Exhibit 8). That share increased quickly, more than doubling to 20.9 percent in 2016, then ranged between 20.3 percent and 25.2 percent of the prescriptions in its drug class from 2017 through 2021. During this period the DWC adopted the MTUS Formulary, which took effect in January 2018. At first, gabapentin enacarbil was not listed in the Formulary, but in October 2018 it was added to the Formulary Drug List with a reference to the ACOEM Guidelines noting that while it is not recommended for anxiety disorders, chronic pain, hip and groin disorders, or PTSD, it is recommended for shoulder injuries, though as a non-exempt drug it is subject to prior authorization.

Exhibit 8: 2015-2024 Calif WC Utilization & Payment Trends, Gabapentin Enacarbil ER (Horizant)

	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
Gabapentin Enacarbil (Horizant)										
% of Psychotherapeutic & Neurological Drug Rx	8.1%	20.9%	25.2%	23.0%	20.3%	23.1%	21.2%	17.1%	11.2%	6.1%
Avg Paid per Rx	$425	$555	$639	$666	$737	$784	$723	$947	$1,003	$969

[19] Young, B., Jones, S. *Cost Driver Medications in the Top California Workers' Comp Drug Groups: Part I, Anti-Inflammatories and Anticonvulsants*. February 2023.
[20] Merlino G, Serafini A, Young JJ, Robiony F, Gigli GL, Valente M. Gabapentin enacarbil, a gabapentin prodrug for the treatment of the neurological symptoms associated with disorders such as restless legs syndrome. Curr Opin Investig Drugs. 2009 Jan;10(1):91-102. PMID: 19127491.
[21] GlaxoSmithKline and Xenoport Receive FDA Approval for Horizant. GlaxoSmithKline press release, April 6, 2011.
[22] GlaxoSmithKline. GSK and XenoPort Receive FDA approval for Horizant for Postherpetic Neuralgia. Press release, June 7, 2012.

% of Psychotherapeutic & Neurological Drug Spend	8.5%	21.9%	29.9%	21.2%	17.1%	18.2%	14.3%	14.4%	10.1%	5.1%

Over the last five years, gabapentin enacarbil's share of the Psychotherapeutic & Neurological Drug prescriptions has continued to fall, declining from 23.1 percent in 2020 to 6.1 percent in 2024, as dextromethorphan HBr quinidine sulfate's share of the prescriptions in this drug group soared. Thus, even though the average payment for gabapentin enacarbil jumped from $784 to as much as $1,003 per prescription within that 5-year span, it remained below the average payment for all prescriptions in this drug group, which combined with its declining share of the prescriptions, drove its share of the Psychotherapeutic & Neurological Drug spend to a 10-year low of 6.1 percent in 2024, so it became far less of a cost driver within its drug group than it had been throughout most of the prior decade.

Once-Daily Gabapentin (Gralise)

Shortly before the FDA approved gabapentin enacarbil in April 2011, it approved another brand-name drug, once-daily gabapentin (Gralise) for the treatment of PHN.[23] Unlike other gabapentin formulations that have been approved for the treatment of conditions such as seizures or neuropathic pain, the FDA only approved Gralise for PHN. As previously noted, PHN is not typically a condition found in workers' compensation because barring a work-related exposure to someone with an active infection (e.g., a nurse in a hospital), or if it is proven that work conditions triggered a shingles outbreak in someone who already carried the virus, shingles is not normally claimed as a work-related disease.

As with Horizant, the IRIS data suggest that in California workers' compensation, Gralise is not typically prescribed to treat PHN, but instead, is primarily prescribed as an off-label treatment for neuropathic or chronic pain related to other conditions. According to the IRIS data on claims in which Gralise was prescribed, the top diagnostic category for claims in which Gralise was prescribed is "diseases and disorders of the spine," with strains, dislocations and fractures being the most common injury descriptions noted for those claims. Approval of Gralise for off-label use is somewhat surprising given that the MTUS Formulary lists it as non-exempt, so it is subject to prospective UR and a showing by the physician that it meets evidence-based clinical guidelines for the specific injury, and the reference to the ACOEM Guidelines in the Formulary Drug list specifies several conditions for which Gralise is not recommended, including anxiety, chronic pain, hip and groin disorders, and PTSD.[24]

Gralise is dispensed in tablet form, and originally, it was only available in 300 and 600 milligram (mg) dosages, though after 2015, 450 mg, 750 mg and 900 mg dosages of the brand drug were approved and made available. The 600 mg tablets represented about 90 percent of the Gralise prescriptions in the IRIS database, and the 300 mg tablets represented about 10 percent, though the number of tablets dispensed

[23] Depomed, Inc. Depomed Announces US Food and Drug Administration Approval of GRALISE Once-Daily Tablets for Treatment of Post-Herpetic Neuralgia. Press release, Jan. 28, 2011.
[24] California Division of Workers' Compensation, MTUS Drug List v.13 (8 CCR § 9792.27.15), Addendum One. Effective August 6, 2025), MTUS Drug List Version 13, p. 14.

per prescription varied widely and was a key variable affecting the amount paid for each prescription. Generic versions of the drug (in 300 and 600 mg dosages) were not approved until early 2024,[25] so the 2015-2023 data in this study reflects the brand version of the drug only.

With no generic version available until 2024, the average payment for Gralise rose from $392 in 2015 to $914 in 2023 (Exhibit 9), but during this period the other high-cost drug in this group, dextromethorphan HBr quinidine sulfate, saw its share of the Psychotherapeutic & Neurological Drug prescriptions more than quadruple, so Gralise's share dropped by half, falling from 53.6 percent to 25.1 percent, and its share of the Psychotherapeutic & Neurological Drug spend fell from 51.4 percent to 20.4 percent.

Exhibit 9: 2015–2024 Calif WC Utilization & Payment Trends, Gabapentin Once Daily (Gralise)

	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
Gabapentin Once Daily (Gralise)										
% of Psychotherapeutic & Neurological Drug Rx	53.6%	46.3%	42.1%	38.4%	40.5%	31.7%	25.5%	23.0%	25.1%	24.7%
Avg Paid per Rx	$392	$478	$528	$614	$708	$827	$818	$895	$914	$583
% of Psychotherapeutic & Neurological Drug Spend	51.4%	41.8%	41.2%	32.7%	32.8%	26.4%	19.5%	18.3%	20.4%	12.6%

Over the past four years Gralise has consistently accounted for about a quarter of the prescriptions within its drug group, but the introduction of generic versions of the drug in 2024 had an immediate effect on the average price. The Institute's Prescription Drug Interactive App shows that in 2024, the average amount paid per prescription for generic gabapentin once daily was $362, while the average payment for the brand version of the drug was $969, so the overall average payment fell from $914 in 2023 to $583 in 2024, driving its share of the drug spend within the drug group down from 20.4 percent to 12.6 percent.

Dextromethorphan HBr Quinidine Sulfate (Nuedexta)

The FDA first approved the combination drug dextromethorphan HBr quinidine sulfate (Nuedexta) 16 years ago for the treatment of pseudobulbar affect (PBA),[26] which as noted earlier is a condition described as "emotional incontinence" marked by uncontrollable and inappropriate laughter or crying

[25] Zydus Lifesciences Ltd. Zydus receives Final Approval from the USFDA for Gabapentin Tablets (Once-Daily), 300 mg and 600 mg (USRLD: Gralise® Tablets) Press release, January 25, 2024.
[26] AVANIR Pharmaceuticals, Inc. "AVANIR Pharmaceuticals Announces FDA Approval of NUEDETA™ Press Release, November 1, 2010.

that does not match how a person feels. PBA occurs as a secondary condition to a variety of otherwise unrelated neurologic conditions. Nuedexta works by modifying brain signals that affect mood and emotions, helping to reduce the number of sudden, uncontrolled reactions that happen with PBA.

During its FDA trial period, the target population for Nuedexta was primarily patients suffering from ALS (Lou Gehrig's Disease) or Multiple Sclerosis, as PBA is a common affliction for these patients, though over the past 15 years research has also shown that PBA can arise from traumatic brain injury (TBI), concussions, strokes, or neurological injuries.[27,28] Because these conditions can be work-related, PBA is recognized by the MTUS and ACOEM as a valid workers' compensation neurological condition, but caution is advised as the quinidine in Nuedexta has cardiac risks and a number of other potential side effects.[29] Dextromethorphan HBr Quinidine Sulfate is listed in the MTUS Formulary as a non-exempt drug, so it requires prior authorization and the prescribing physician must provide a clinical rationale for using the drug for the specific injury. Furthermore, the MTUS Formulary Drug List's reference to the ACOEM Guidelines for Nuedexta notes that the drug is not recommended as a treatment for TBI.[30]

Nuedexta has never been approved by the FDA for anything other than PBA, and a review of the IRIS data on claims in which this drug was prescribed reveals that the diagnosis codes on many of the claims do indicate head, cranial and intracranial injuries or diseases of the nervous system, so in these cases PBA may have been diagnosed and use of Nuedexta may have been appropriate.

Other claims, however, involved diagnoses such as fractures of the lower extremities or trauma related to joint diseases and disorders, while the injury codes included strains, amputations, and COVID-19. This suggests that the drug may have been prescribed as an off-label treatment for conditions other than PBA caused by neurological injury or disease. Any off-label prescribing of this drug should raise a red flag for claims administrators, UR professionals and PBMs, and merit a discussion with the prescribing physician as use of Nuedexta in claims involving conditions other than PBA is not supported by the ACOEM/MTUS Guidelines.

Off-label prescribing of Nuedexta should be particularly concerning in light of federal investigations within the past decade that led to sanctions against the drug manufacturer for false and misleading marketing (particularly to long-term care facilities), alleged kickbacks, and off-label promotion of the

[27] Brooks, B. R., Thisted, R. A., Appel, S. H., Pioro, E. P., & Cummings, J. L. (2016). PRISM II: an open-label study to assess effectiveness of dextromethorphan/quinidine for pseudobulbar affect in patients with dementia, stroke, or traumatic brain injury. BMC Neurology, 16, 105. https://bmcneurol.biomedcentral.com/articles/10.1186/s12883-016-0609-0
[28] Mayo Clinic. (2025). Pseudobulbar affect (PBA). Mayo Clinic. https://www.mayoclinic.org/diseases-conditions/pseudobulbar-affect/symptoms-causes/syc-20353737
[29] The drug manufacturer's information on contraindications for Nuedexta notes that it is contraindicated in patients with a prolonged QT interval, congenital long QT syndrome, history suggestive of torsades de pointes, heart failure, patients receiving drugs that both prolong QT interval and are metabolized by CYP2D6 (e.g., thioridazine and pimozide), patients with complete atrioventricular (AV) block without implanted pacemaker, or at high risk of complete AV block. Important Safety Information and Indication for Nuedexta. Otsuka America Pharmaceutical, Inc., July 2025.
[30] MTUS Drug List v.13 (8 CCR § 9792.27.15), p.9. ACOEM Guidelines Copyright Reed Group Ltd. Effective Aug 6, 2025.

drug. These included whistleblower suits in Ohio[31] and Georgia,[32] and a $95 million False Claims Act settlement and a $103 million settlement for promoting the drug for uses other than PBA.[33] The main federal actions and sanctions were resolved in 2019, with the underlying investigation covering conduct up through 2016-2017. However, given that dextromethorphan HBr quinidine sulfate is classified as a non-exempt drug and the history of aggressive marketing of the drug for off-label use, requests for this drug should be reviewed carefully.

Despite these issues, Exhibit 10 shows that dextromethorphan HBr quinidine sulfate has been the fastest growing Psychotherapeutic & Neurological Drug in California workers' compensation over the past decade as its share of the prescriptions within its drug group quadrupled from 8.4 percent in 2015 to 35.9 percent in 2024.

Exhibit 10: 2015–2024 Calif WC Utilization & Payment Trends, Dextromethorphan HBr Quinidine Sulfate (Nuedexta)

	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
Dextromethorphan HBr Quinidine Sulfate (Nuedexta)										
% of Psychotherapeutic & Neurological Drug Rx	8.6%	10.9%	12.5%	14.1%	12.5%	15.9%	25.8%	38.2%	37.3%	35.9%
Avg Paid per Rx	$659	$739	$774	$962	$1,118	$1,224	$1,248	$1,214	$1,222	$1,317
% of Psychotherapeutic & Neurological Drug Spend	13.9%	15.1%	18.0%	18.9%	16.0%	19.6%	30.1%	41.3%	40.7%	41.2%

At the same time, Nuedexta remains under patent, so less costly generic versions of dextromethorphan HBr quinidine sulfate have not been available. As a result, the average amount paid per prescription for this drug doubled from $659 in 2015 to $1,317 in 2024, so its share of the Psychotherapeutic & Neurological Drug spend tripled from 13.9 percent to 41.2 percent over that 10-year span, making it the key cost driver in its drug group during the study period.

[31] United States ex rel. Kevin Manieri v. Avanir Pharmaceuticals, Inc. — Civil whistleblower suit in the Northern District of Ohio. Action No. 5:15-cv-611 (N.D. Ohio).
[32] United States ex rel. Duane Arnold and Mark Shipman v. Avanir Pharmaceuticals, Inc. — Civil whistleblower suit in the Northern District of Georgia. Action No. 1:15-cv-01250 (N.D. Ga.).
[33] Pharmaceutical Company Targeting Elderly Victims Admits to Paying Kickbacks, Resolves Related False Claims Act Violations, U.S. Dept. of Justice News Release, September 26, 2019.

Summary

This report extends CWCI's research series that began in three years ago with a look at low-volume, high-cost drugs in California workers' compensation. The latest analysis focuses on Psychotherapeutic & Neurological Drugs—an infrequently used drug group that represents a tiny share of all prescriptions dispensed to injured workers, but that has emerged as one of the top ten costliest drug groups in California workers' compensation due to the use of high-priced, specialty medications. As a result, total payments for this group are now approaching those of Opioids and Antidepressants.

A review of recent trends within the Psychotherapeutic & Neurological Drug group shows that since 2018—the first full year following the implementation of the MTUS Formulary and incorporation of ACOEM's Opioid and Pain Management Guidelines into the MTUS—the steady increase in the Psychotherapeutic & Neurological Drugs' share of the workers' compensation total drug spend has coincided with a shift in the distribution of the prescriptions and payments within the drug group.

Together, the two least expensive drugs highlighted in this report, memantine HCl (Namenda) and donepezil hydrochloride (Aricept), both of which are available as generics, saw their share of the prescriptions within the drug group more than double from 10.6 percent in 2018 to 26.2 percent in 2024; however, due to their relatively low cost, their share of the Psychotherapeutic & Neurological dollars has remained below 1 percent since 2018, ranging between 0.3 percent and 0.9 percent. On the other hand, both gabapentin enacarbil (Horizant) and gabapentin once daily (Gralise) have represented a declining share of the prescriptions and the total drug spend within the drug group, as their combined share of the prescriptions dropped from 61.4 percent in 2018 to 30.8 percent in 2024, while their combined share of the Psychotherapeutic & Neurological Drug payments fell from 53.9 percent to 17.7 percent. Meanwhile, dextromethorphan HBr/quinidine sulfate (Nuedexta) has become the key cost driver in this category as its share of the prescriptions within the drug group rose from 14.1 percent in 2018 to 35.9 percent in 2024, and with average payments for the drug increasing from $962 to $1,317, its share of the Psychotherapeutic & Neurological Drug spend surged from 18.9 percent to 41.2 percent.

Given their consistently tiny share of workers' compensation prescriptions, little attention has been paid to Psychotherapeutic & Neurological Drugs, but their increasing share of the total drug spend—now 3.4 percent, a nearly 5-fold increase since 2015—should serve as a red flag to claims administrators, PBMs, and utilization reviewers to keep an eye on these medications, especially the brand name drugs which now account for 7.0 percent of all brand-name drug payments in the California workers' compensation system. Careful review of the types of injuries for which these drugs are requested is warranted to ensure that the underlying condition is work-related and that these drugs are appropriate and consistent with nationally recognized treatment guidelines. This need is heightened by the potential side effects and risks associated with drugs in this group, the high cost of several of them, and the history of aggressive marketing and off-label use of Nuedexta, which within the past decade has been the subject of whistleblower suits and federal and state actions that resulted in more than $100 million in legal settlements.

CWCI will continue to monitor the utilization and reimbursement of Psychotherapeutic & Neurological Drugs and report back in future studies and through our online application, which is updated twice a year and available to CWCI members in the Research section at www.cwci.org.

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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 70 percent 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 at www.cwci.org. The Institute is not affiliated with the State of California.

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