Workers' Comp

New Trends in Opioids and Pain Management

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Tom Kerr (TK): On today's podcast, we'll be discussing part 3 of Enlyte's Drug Trends Report. The information for this section focuses on the opioid therapeutic class. It reviews data billed through Enlyte Pharmacy Solutions in 2022 and 2023 where both in-network and out-of-network prescriptions were available for analysis. Talking with me today is the lead author of that report Nikki Wilson. Nikki, thanks for joining us.

Nikki Wilson (NW): Yes. Glad to be here.

TK: So, 2023 saw declining trends overall in opioid utilization and spend, along with continued reductions in MED. Let's talk about some of the medications behind those numbers that were driving the activity within the class.

NW: So, looking at our aggregate trends among our top five opioid medications by cost, across, both retail and mail order channels, as well as our out of network or medical bill, paper bill prescriptions, we see a list that includes oxycodone, hydrocodone, and tapentadol products. And these meds represent the majority of the opioid scripts and costs for 2023, accounting for 63.7% of costs and 52.3% of usage associated with the therapeutic

class.

And their activity can offer further insight into the favorable trends experienced among this impactful category that we continue to carve out separately for additional analysis. So, we're continuing to really focus in on the opioid class.

The oxycodone products holding the top spots overall for cost are OxyContin, which is a controlled?release or long?acting version of oxycodone, and the combination product or immediate?release oxycodone and acetaminophen products which took the top spots, both tied at about 21.8% of total opioid cost.

Oxycodone/acetaminophen's cost percentage was due, in part, to the volume of prescriptions represented in the category that includes generic versions of common branded products such as Percocet and Endocet. OxyContin remains largely dispensed as a brand medication today. So, while the volume was comparatively low when looking at the other opioids in the top five, at only 5% of total scripts for opioids, it was still high enough to secure that top spot based on its cost.

I'm going to jump on to the hydrocodone/acetaminophen products. Those held the No. 4 spot by cost, and they remain the top opioid medication by utilization within that drug class, making up just over a quarter of total opioid scripts at 29.4% and about 6.5% of total opioid cost. This category includes generic versions of common brands, Vicodin, Norco, Lortab. There's a handful of others, but they're very popular opioid medications overall.

Then the remaining two meds rounding out the top five opioid spots, ranked by cost, at the No. 3 and No.5 spots respectively, are both brand?only tapentadol products, Nucynta and Nucynta ER. Nucynta actually first showed up in our top five fairly recently, a few years back in 2019. In 2023, both Nucynta products are currently only available as brand?name medications, which does contribute to that larger cost share, with expected patent protections expected to expire for both the immediate?release and extended?release Nucynta products in mid? to late?2025.

So that would allow for the introduction of generics. Then, of course, we would expect costs to trend downward over time once that happens. In terms of utilization, Nucynta is lower comparatively. It ranks about No. 8 by number of prescriptions. This gives some insight into how that higher price tag currently associated with brand Nucynta products drives it up the list in terms of opioid cost ranking.

Interestingly, tapentadol has a fairly unique mechanism of action among opioids that might make it a good clinical choice for patients who are candidates for an opioid with some nerve?related pain component. It is a dual action analgesic, similar to the way that tramadol works, which we used to consistently see in our top five.

This is sort of the thing that's come in to take its place, as that branded medication bumps it to the top in cost. But they are both opioid agonists, so they work on those opioid receptors like every other opioid. But they also have some action at the norepinephrine receptors. They inhibit the reuptake of that particular neurotransmitter. It's kind of considered like oxycodone mixed with Cymbalta. It works a little bit that way.

And we know the pathophysiology of neuropathic pain, where evidence has shown that the body's internal neurotransmitters, such as norepinephrine, serotonin, various endorphins, those are all down regulated in neuropathic pain or nerve?related pain.

So, any meds that lead to more of those neurotransmitters being released or staying active in the nervous system or that pain pathway, can lead to improved pain management. So that's an interesting thing about tapentadol, which seems to have effects on that norepinephrine component.

The last thing to note when we're looking at trend changes among those top five opioid medications is that all five experienced declines in scripts per claim compared with the previous year, and most dropped in cost per claim as well. Total opioid utilization fell by 10.1% per claim and cost dropped by 4.8% per claim from 2022 to 2023, with the top five opioids representing an 11.5% and 4.5% decrease in those same categories.

TK: And, even with the decreases experienced within the opioid class related to scripts per claim and cost per claim, we continue to highlight this therapeutic class. Why is this category still considered among the so?called high?impact drug classes when we look at the trend data?

NW: Opioids, they remain our No. 1 class by utilization in workers' compensation. That's been pretty consistent. So, we're certainly focused on them just because of the sheer volume and the number of patients that we're treating and managing that are using these medications.

And statistics have shown us, and I think everyone is well aware of this stat at this point, that the leading cause of accidental death in the US among adults is drug overdose, and a number of those overdoses is attributable to opioids. So, they are not without very serious risks.

So, there's a lot of importance there to still track and ensure we're stewarding those drugs responsibly. We do know that overdose is a concern. We know that the No.1 drug class for workers' comp is opioids. As a percentage of all the scripts that were processed in 2023, they make up about 21% of that volume.

So, they're the top, followed by NSAIDs, non?steroidal anti?inflammatory drugs, which are also for pain. And there's four other pain?related medications in that top five by utilization. So, pain is definitely an issue, something that we're looking at.

So, we know that overdose is a concern with opioids, but certainly, those meds come with a myriad of additional risks and considerations, including legal and social impacts. So, to put this in perspective, yes, we certainly want to prevent an overdose or a death, but there's a number of other things that we should be looking at.

And pulling from several statistics and studies on the topic of opioids and substance use disorder in the US that have been put forth by various agencies, like the Centers for Disease Control and Prevention, SAMHSA, who does the National Survey on Drug Use and Health, stratifying those out for every one opioid?involved overdose deaths, there were 114 people who reported misuse of opioids in the past year.

There are 298 people who met the *Diagnostic and Statistical Manual*, or the *DSM?5*, criteria for substance use disorder diagnosis related to drug use, of which we have research that has also shown that this population is grossly under?treated, with only about 6% of adults 12 and older with substance use disorder receiving treatment.

And beyond that, for every one opioid?related death, there are 576 people over the age of 12 who reported substance use disorder in the past year, either alcohol or drug-related.

So, there's definitely a larger fallout and a larger onus for us to be monitoring, managing this category, not only for some of the safety risks that are out there, but some of the impacts that it can have on overall mental health and just quality of life.

TK: We've seen and mentioned already that, year over year, opioid volumes and cost have declined. What are some approaches that can be deployed to help ensure that when opioids are used, that utilization is appropriate?

NW: Yes, so important. And we do have a number of guidelines that give us help in this arena, but, you know, there was a moment where the CDC put forth some recommendations based on a number of research input from various clinicians and almost got their hands slapped because the guidelines were taken too strictly or verbatim and were causing some treatment concerns across the nation.

So, they had since revamped those. Their first controls came out in 2016, and a number of years later, they published updated guidance again, sort of making it clear that these are a guide so that do not replace that prescriber?patient relationship, and everything must be considered as a one?off. But it does give us some good guardrails and some considerations.

Beyond that, there are several other national organizations that have produced evidence?based recommendations. So that's exactly what they do — focus on when to prescribe opioids, when to continue or discontinue opioids, the appropriate durations of use according to injury type, dosing limitations, when to involve a pain specialist, how to identify whether a patient is a candidate in the first place for opioid therapy, what to monitor throughout treatment with opioids, and then how to manage some of those side effects.

And some of those guidelines are state?specific. Famously, New York's Medical Treatment Guidelines have been developed by their workers' compensation board and are now driving a lot of prescription?related care in that state.

California's Medical Treatment Utilization Schedule, which was created under the Division of Workers' Compensation, also represents another example which provides specific guidance around a number of drugs, including opioids, when to request utilization review, etc.

Some states impose opioid?related regulations around dispensing or enforce closed formularies that help to guide drug selection. And published guidance is also available from various medical societies, including the American Pain Society, the American Academy of Pain Medicine, and the American Society of Anesthesiologists.

We are at no lack of guidance on this very important topic, for a drug that can be very risky, but can also be very effective in pain management. I mentioned the US Centers for Disease Control and Prevention, their published guidance was focused on prescribing opioids for chronic pain, an arena that we really didn't have a lot of help with previously.

Most of the opioids being used were for cancer pain and for acute pain. They had a mobile app that they had created aimed at helping prescribers adhere to those guidelines. And, and there's also others available from workers' comp?specific national entities, such as the American College of Occupational and Environmental Medicine, or ACOEM, as well as from the Work Loss Data Institute. And that's the company behind the Official Disability Guidelines, or ODG.

TK: So how do these guidelines help providers determine when opioids should or shouldn't be prescribed?

NW: Many of the resources offer guidance and outline what should take place if prescribers identify risks or if an opioid overdose occurs. And a lot of those also address opioids placement therapy and other treatment options.

Some of the major recommendations that we find across those various guidelines related to pain management, opioids, are not generally indicated for non?severe pain or for the treatment of chronic or non?cancer pain. And also, there's really little to no evidence of long?term benefit for those uses for chronic and non?cancer pain, but that doesn't mean they aren't used.

So, one of the recommendations is to use alternative analgesics or other non?opioid medications as part of pain management wherever possible to explore non?drug approaches. There's a lot of those like cognitive behavioral therapy, acceptance therapy, yoga, meditation, relaxation strategies, or a combination of those. Exercise. It's just patient?specific.

But if opioids are used, and there is a time and a place for these, the goal should be to focus on improvements. Yes, the injured employee's level of pain, but also function should be a huge point of focus, especially in our comp population where there's typically an injury that's prevented return to work. That's a really important goal to establish.

And then, frequent evaluation for harms and benefits of the opioid should occur. The prescriber should be remaining engaged with the patient, not treating in a vacuum, understanding the impacts of any of that patient's biopsychosocial factors — so, their living situation at home, what mental health disorders might they have that might put them at more risk? What can we do from a full patient treatment perspective to ensure the best outcomes?

And that includes regular follow ups and check-ins. Discussing those alternatives for treatment beyond opioids, continuously looking for improvements in function or rehabilitation or return to work versus solely a pain focus and really partnering with that patient if opioid treatment programs for recognized opioid use disorder are needed.

TK: What do the guidelines say about minimizing risks and promoting safety in using opioids?

NW: Prescribers should be following those best practices that we just outlined to mitigate risks associated with opioid use by prescribing the lowest effective dose and making slow increases as necessary with morphine equivalent dose of 50 or less recommended for all opioids prescribed.

As we know, risk has been shown to increase above that dose. We have seen a number of MED threshold recommendations vary where various guidance do not recommend going above and beyond. Typically, they choose a value around 90. The CDC and ODG looks at that and it aligns closely with what Enlyte uses as a risk factor computation as well.

Beyond that level, the risk increases exponentially. So, it's not a hard?and?fast cutoff, but it is an indicator of when we should pay more attention, perhaps consider, referral to a pain specialist, etc.

Other recommendations include frequent review of the state's prescription drug monitoring program. Those capture and track all the Schedule II substances that are typically dispensed in a state beyond just comp. It's anything that's coming through.

So, if the patient paid cash or if the patient went through a different insurance, the opioid would show up in that monitoring system. So, it's a good check for the prescriber before they themselves start prescribing opioids on top of what might also be out there.

Utilization and deployment of urine drug testing, regular evaluations as we mentioned a little bit earlier, substance use disorder, particularly opioid use disorder, but any substance use disorder can increase risk for having an issue.

And consideration for naloxone, which is that opiate overdose reversal agent. Just having it prescribed, having it in the hands of the patient, especially if they're at an increased risk, or if they have kids at home or they're taking a number of other drugs that can increase the risk of overdose, that's a good thing to help decrease the incidence

of death from overdose there, just another risk mitigation strategy.

So, considering the potentially increased risk from other central nervous system depressant meds the patient is taking and avoiding prescribing those while the patient's using opioids, that's another recommendation

You have to consider everything the patient might be using that could be depressing that central nervous system. That's how overdose occurs. the central nervous system, is slowed down to such a degree that the patient stops breathing.

Alcohol or other illicit substances that do that, or the presence of comorbid conditions such as those that already impact a patient's breathing, like sleep apnea, COPD, mental health disorders, those have all shown an increased risk with opioids.

So, education really goes a long way just in making sure that patient understands everything I described, what to look for while they're on opioids, where to get support if they start having an issue, what are the alternative treatment options.

TK: What can payers and TPAs do to support these guidelines?

NW: Opioid management strategies to consider for payers, insurers, TPAs, those that are responsible for managing pharmacy benefits, is look for ways you can promote adherence to those best practice prescribing that I just went through.

Look for ways to limit physician dispensing and repackaging drugs, so that you can apply appropriate clinical management and consider safety and risk controls before that medication's in the hand of the patient. Establish and enforce drug formularies where they don't exist by state so that you have some additional protections.

Monitor for at?risk individuals. We know what is associated with increased risk, so put in controls for monitoring that. Look for opportunities for early intervention. The longer a patient's on opioids, the risk goes up. We want to be able to get in front and maybe educate early on. Ensure any of those evidence?based recommendations that we just talked about are followed for ongoing opioid therapy.

And then, if you need to refer patients for a drug utilization review, there's formal UR, available in many states. There's also things like a physician peer review that can be requested, usually a fee for service that can be very effective to engage that prescriber.

And then, engaging the clinician to consult with the treating physician and/or the patient themselves, whether that's a case manager, or like I said, a peer review, that can be very effective as well.

And partnering with the PBM. I mean, that's what we do all day long at Enlyte for pharmacies. A lot of these things are built into our clinical programs already. So, it's just a really smart move to ensure you have those strategies in place.

TK: Great. So, given the increased focus around the management of opioids and their potential pitfalls, what are some of the available alternatives for pain management?

NW: That is a great question. There's so much focus, I think, especially since opioids really came into the spotlight when overdose deaths were really spinning out of control.

That was sort of the golden ticket, how do we find a drug that is just as effective as opioids, but doesn't lead to the same addiction potential or the same euphoria? Can we create a euphoria?sparing analgesic that targets those

same pathways, and what have you?

And I can tell you, the pain pathway itself is a fascinating system within the body, and it has a number of potential targets, a number of potential levers to pull to provide pain relief. There are medications already FDA? approved and on the market that can work at a number of those different sites within the body and have different mechanisms of action and, of course, different side effects, different tolerability, different risks to consider.

So, it's really sort of a balancing act of figuring out what's most appropriate for that patient, what type of pain are we dealing with? Your treatment choice might be different if you're dealing with a peripherally acting pain type. So, it's at the point of injury.

So, I have pain in my elbow that I just broke, a non?steroidal anti?inflammatory drug might be a good idea there. That's not working? Maybe a topical like capsaicin, or maybe, I'll have to move to tramadol or one of the opioids, because they work well for acute pain at that site. And then it might be a different decision if it's peripherally acting along the nerve. So, if we've got nerve?related pain now, we move to a different grab bag of so?called adjuvant analgesics.

So those that are on the market, not necessarily to treat pain but they can be effective in pain management, partly because of some of what I described earlier with the different neurotransmitters that are at play in that pain cascade things that can improve pain outcomes, like, increase norepinephrine or increase serotonin.

So, the gabapentinoids fall there. So, things like gabapentin or Neurontin, that's an anticonvulsant originally on the market for seizures, but we found them to be effective in nerve?related pain. Local anesthetics can be helpful there as well or injectable anesthetics. So, it just really depends on the type of pain complaint. But there's a number of things already on the market including basics like Tylenol or acetaminophen, and aspirin. Those are all non?opioid analgesics with great potential for efficacy.

And, in fact, a lot of opioids are combined with acetaminophen, and it does a good job of dealing with those pain complaints. And if those don't work, you move up the ladder to stronger and stronger products.

Topicals have really become an area of focus. We've seen a shift in our trends, for certain, on those really rising in utilization and in spend. They did bump opioids off the top spot overall for costs in 2023 and 2022. They took that No.1 spot because we're seeing a number of costly products fall there as well.

Some of the topical NSAIDs, like Pennsaid or Flector Patch or Voltaren gel, which is now available over the counter are good, targeted therapies for various joint pain and different types of pain that are out there. We have others that are being used, like anesthetics and lidocaine. But then there's a number of very expensive private label topical analgesics that have the same or similar ingredients to over?the?counter creams and ointments like Bengay or Icy Hot or Thera?Gesic that are being marked up considerably and marketed directly to physician offices for dispensing. So that's an area, certainly, to watch.

But there's a grab bag of different very non?invasive topical products that could be a good choice for pain, especially given the low incidence of side effects, because it's nothing the body is ingesting to as great of a degree as when you're taking a medication by mouth.

Steroids also are powerful anti?inflammatories, antidepressants off?label, used a lot for chronic and nerve? related pain.

And we have a grab bag of other targeted therapies. So, things like musculoskeletal pain, you can get a muscle relaxant if it's thought to be effective for that. Intra?articular injections like Euflexxa or Synvisc or Orthovisc,

where you've got a knee complaint and you're trying to avoid total knee replacement. They are indicated as a first step where you directly inject the joint for increased lubrication of that viscose supplementation, basically, of that cartilage that's in the knee to help improve cushioning and lubrication there.

Even basic things like anti?infectives can help with pain complaints. And even psych meds. There's, sort of a cyclical relationship between chronic pain and depression, and improving one tends to improve the other.

TK: Has there been anything newly developed within the space, or is anything in the pipeline?

There's a number of other developments. We've seen an increase in the use of local anesthetics or peripheral nerve blocks for pain complaints. So, things like bupivacaine, lidocaine, procaine tetracaine, where they work in different pathways along that pain pathway.

As I was saying, usually quick action, and often these types of blocks or nerve blocks can last a long time. There was one that was being used, for post?surgery, in dental work, that was creating a block that lasted up to 72 hours, and it greatly minimized the need for any type of opioid or strong pain medication going home with that patient if it was given at the time of the procedure.

So, there's just some great promise there for helping to assist and decrease use of opioids.

Neurotoxins, another area of development, things like Botox, or botulinum, toxin products, Dysport, Myobloc, Xeomin, most of those are used for muscle spasticity. So, there's a role that they might play. They're being investigated, and some are FDA?approved for headaches and other things of that nature when other treatments don't work.

And then there's a lot of exploratory interest in things like tetrodotoxin, which comes from the pufferfish, and resiniferatoxin, which comes from a type of cactus. And they work through a sodium channel inhibition and through a receptor called TRPV1, which is a similar pathway that capsaicin uses to help provide pain relief. So, lots of exploring there.

There is a drug on the market, Prialt, which is made from a neurotoxin from snails, a conopeptide agent. And it's an injectable that's FDA?approved for pain. There's pharmacotherapeutic targets that are being explored that we know are in that pain pathway, and drugs are being researched currently to see what might be occurring with those. A number of them look at voltage?gated sodium channel inhibition.

Suzetrigine is an investigational drug that is being explored right now and is going through clinical trials. It's looking very promising in that area. "Might replace opioids" is what all the headlines say … we'll see, but there's some promise there.

Oliceridine is another type of drug that's on the market today that represents a target that's being explored. G?protein?coupled receptor drugs are being explored because, they are very effective. They include opioids, but they also include histamine receptor blockers, beta blockers, angiotensin receptor blockers.

TK: Are there other drug classes that target chronic pain relief?

NW: Of course, we've talked a little bit about in our drug trends, those calcitonin gene?related peptide inhibitors that are on the market now for migraine relief, Aimovig, Nurtec. That's another unique drug category or drug target that has recently come to market that's sort of a groundbreaker in the treatment of migraine pain.

The last two I'll mention are endocannabinoid receptor agonists and, of course, our five hydroxytryptamine or serotonin receptor agonists. Like any of the psychedelics that are being explored right now, these have an effect

on serotonin. And so, they're being looked at for a number of different uses, but things like magic mushrooms or psilocybin are being explored there.

And, beyond that, we have a whole category that isn't even medication-related. It's digital therapeutics, where we have specific digital health apps that are targeting pain. One example is Abbott's Patient Controller and Enlyte's app that's used in conjunction with their neuromodulation devices, or others are used in conjunction with some sort of drug therapy, to keep the patient compliant with their medications or to help them improve their range of motion when they're going through pain.

It's fascinating to see where we're headed. There's a lot of options that are coming down the pipeline, understanding the issue that our country has with pain treatment and some of the risks that opioids possess. So, we'll continue to watch those as we go.

TK: Thanks, Nikki. And for more information on the Enlyte Drug Trends report as well as more detailed interviews with Nikki Wilson's analysis, visit www.enlyte.com/drug-trends. Until then, thanks for listening.



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