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Drug Class Update: Analgesics

Date of Review: April 2026

Date of Last Review: Non-steroidal anti-inflammatory drugs (February 2021)
Opioids (April 2021)
Muscle relaxants (September 2019)
Topical Pain Medications (August 2020)
Suzetrigine (June 2025)
Dates of Literature Search: 01/01/2021 – 02/13/2026

Current Status of PDL Class:
See **Appendix 1**.

Purpose for Class Update:
Evaluate new comparative evidence of oral analgesics (opioids and non-opioids) including evidence for pain conditions that are currently unfunded.

Plain Language Summary:

- Many social and medical factors contribute to acute and chronic pain. In most cases, pain should be treated with more than one type of treatment with the goal of reducing, not eliminating, pain.
- Common types of medicines used to treat pain include non-steroidal anti-inflammatory medicines (NSAIDs), acetaminophen, opioids, muscle relaxants, suzetrigine, and topical pain medicines that are applied to the skin. Evidence shows that medicines also used for depression or seizures can improve certain types of pain.
- There is little evidence that one specific medicine improves pain more than another medicine of the same type.
- New evidence showed that certain types of pain medicines may have benefit over other types of pain medicines for specific people:
  - NSAIDs may be more effective compared to acetaminophen for acute pain after surgery in children or compared to opioids after breast surgery in adults.
  - Most medical organizations recommend antidepressants as an initial treatment option for pain lasting longer than 3 months.
  - When opioids are prescribed for long-term pain treatment (>3 months) they can cause serious side effects and may worsen pain.
  - Medicines for seizures or depression can improve nerve pain.
  - NSAIDs can improve pain caused by swelling in conditions like gout or arthritis.
- For people already taking opioids long-term for chronic pain, patients and providers should discuss risks and benefits for gradual dose reduction and develop a plan to manage pain and risks related to opioids. Evidence shows that gradual dose reduction of opioids is most successful when offered with high intensity support programs involving multiple providers and treatments.

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Research Questions:

1. What is the comparative efficacy and effectiveness of non-steroidal anti-inflammatory drugs (NSAIDs), opioids, acetaminophen, suzetrigine, muscle relaxants, and topical medications for acute and chronic pain?
2. What are the comparative harms of NSAIDs, opioids, muscle relaxants, and topical medications for acute and chronic pain?
3. Are there subgroups of patients based on demographic characteristics (e.g., age, race, ethnicity, socioeconomic status), concurrent medications, comorbidities, or pregnancy for which there are differences in the benefits and harms of NSAIDs, opioids, muscle relaxants, and topical medications for acute and chronic pain?

Conclusions:

Acute pain

- In acute post-operative pain in children and adolescents,
    - ibuprofen had small improvements in pain intensity with 24 hours following surgery compared to acetaminophen (moderate certainty evidence).[1]
    - ibuprofen was associated with fewer adverse events than opioids (moderate certainty evidence) or ketorolac (low certainty evidence).[1]
    - diclofenac was associated with less nausea/vomiting but increased risk of bleeding compared to opioids (moderate certainty evidence).[2]
- In acute post-operative pain related to breast surgery, NSAIDs may reduce pain intensity within 24 hours, reduce need for rescue opioid use, and decrease risk of nausea/vomiting compared to opioids (low to moderate certainty evidence).[3] NSAIDs use was not associated with risk of breast hematomas compared to opioids (low certainty evidence).[3]
- There was no new comparative evidence identified for suzetrigine in post-operative pain or other acute pain conditions.
- For treatment of acute gout flares, non-selective NSAIDs (e.g., indomethacin, naproxen) have similar symptom improvement compared to selective COX-2 inhibitors (e.g., celecoxib) or glucocorticoids (low to moderate certainty evidence), but may be associated with more adverse gastrointestinal adverse events and withdrawals due to adverse events (moderate certainty evidence).[4]
- In pain related to acute otitis media, there is insufficient evidence to determine differences in efficacy or safety between ibuprofen or acetaminophen.[5]
- In infants who use ibuprofen or acetaminophen as needed for acute treatment of fever or pain during the first year of life, there is no difference in the incidence of eczema or bronchiolitis at 1 year (moderate quality evidence).[6]
- In acute low back pain (<4 weeks in duration), NSAIDs are recommended by the Veterans Administration/Department of Defense (VA/DOD) and National Institute for Health and Care Excellence (NICE).[7,8]

Cancer-related Pain

- In people with pain related to cancer, there is no difference in pain relief with controlled-release oxycodone and controlled-release morphine (low certainty evidence).[9] There was insufficient evidence to evaluate differences in safety or efficacy between other opioids.[9,10]

Chronic Pain (typically defined as pain lasting longer than 3 months)

- There was insufficient evidence to compare efficacy or safety of specific agents within each class of medications for treatment of chronic pain. Guidelines include recommendations based on medication class or for specific agents that had supporting evidence of benefit. For chronic pain, medications should be offered in conjunction with non-pharmacologic and psychologic therapies.
- Antidepressants

    - The Scottish Intercollegiate Guidelines Network (SIGN) recommends duloxetine in people with chronic non-cancer pain, and the VA/DOD recommends duloxetine for chronic low back pain.[8,11]
    - NICE recommends antidepressants (specifically amitriptyline, citalopram, duloxetine, fluoxetine, paroxetine or sertraline) in adults with chronic primary pain.[12]
    - NICE recommends duloxetine or amitriptyline for chronic neuropathic pain, and the American Academy of Neurology (AAN) recommend serotonin norepinephrine reuptake inhibitors (SNRIs; duloxetine, venlafaxine, and desvenlafaxine) or tricyclic antidepressants (TCAs; amitriptyline, nortriptyline, imipramine) for treatment of painful diabetic neuropathy.[13,14]
- Opioids
    - Guidelines from multiple organizations recommend against offering opioids for all types of chronic non-cancer pain.[7,8,12-18] Direct and indirect evidence suggests that individual opioids are similarly ineffective for chronic pain management (low to very low certainty evidence).[18]
    - Use of opioids up to 3 months should be prescribed only when alternatives have been fully explored and benefits outweigh risks.[7,14,18]
    - When opioids are prescribed, appropriate monitoring, risk mitigation strategies, frequent evaluations, and patient-centered collaborative approaches to medication tapers are recommended.[16,18,19] Consider prescribing naloxone for people prescribed opioids who may be at risk of an opioid overdose. When available, interdisciplinary or multidisciplinary care, or multimodal approaches that emphasizes non-pharmacological and self-management strategies to deprescribe opioids are recommended.[16,18,19]
    - In people with severe opioid use disorders (OUD), there is moderate quality evidence that deprescribing alone, without access to long-term substance use disorder treatment and care, is associated with increased risk of overdose and death.[19]
    - For people on chronic daily opioids, the VA/DOD suggest use of buprenorphine instead of a full opioid agonists because of potential for lower risk of overdose or misuse (weak recommendation for treatment).[16]
- Muscle relaxants
    - Guidelines from VA/DOD suggest against offering muscle relaxants for chronic low back pain lasting longer than 4 weeks.[8]
    - NICE recommends baclofen as an initial treatment option for spasticity and pain related to multiple sclerosis (MS).[17]
- NSAIDs
    - The American Academy of Orthopedic Surgeons (AAOS) recommends topical or oral NSAIDs for adults with knee osteoarthritis to improve pain and function.[15]
    - The VA/DOD and NICE recommend NSAIDs for acute or chronic low back pain lasting longer than 4 weeks.[7,8] Because of risk for adverse events with chronic use, they recommend the lowest effective dose for the shortest time with appropriate monitoring and gastroprotective treatment (e.g., antacid medications).[7]
    - NICE recommends against use of NSAIDs for chronic primary pain.[12]
- Other topicals
    - For neuropathic pain, capsaicin is an alternative option for people who cannot tolerate oral therapies (low certainty evidence).[13,14]
- Antiepileptics
    - NICE recommends against use of antiepileptics for chronic primary pain or low back pain.[7]
    - NICE recommends carbamazepine for initial treatment of trigeminal neuralgia.[13]
    - NICE and AAN recommend gabapentinoids (e.g., gabapentin, pregabalin) as initial treatment for neuropathic pain or peripheral diabetic neuropathy.[13,14] AAN also recommends sodium channel blocker antiepileptics (e.g., carbamazepine, oxcarbazepine, lamotrigine, valproic acid, lacosamide) as initial treatment in painful diabetic neuropathy based on moderate certainty evidence.[14] NICE recommends against antiepileptics for neuropathic pain unless prescribed in consultation with a specialist.[13]

- NICE recommends gabapentin as a second-line treatment (e.g., after trial of a muscle relaxant) in people with spasticity and pain related to multiple sclerosis.[17]

Recommendations:

- No changes to the preferred drug list (PDL) are recommended based on the clinical evidence.
- Update opioid, NSAID, and muscle relaxant prior authorization (PA) criteria to align with current evidence for chronic pain conditions (**Appendix 1**).
- After evaluation of costs in executive session, the following products were made preferred:
  - tizanidine 2, 4, 6 mg capsules
  - piroxicam capsules, naproxen sodium capsules, indomethacin ER capsules, and diclofenac ER 24H tablets
  - ketorolac tablets with maintenance of the current quantity limits
  - tramadol ER 24H tablets
  - lidocaine ointment and capsaicin lotion
  - acetaminophen drops, tablets, capsules, ER tablets, rapidis tablet, chew tablet, elixir, liquid, and 160mg/5mL oral suspension
  - aspirin-caffeine, acetaminophen-caffeine, and combination aspirin/acetaminophen/caffeine tablets
- After evaluation of costs in executive session, the following products were made non-preferred:
  - ibuprofen 300 mg tablets
  - morphine sulfate solution, hydrocodone-acetaminophen solution, codeine sulfate tablet, butorphanol tartrate spray, hydromorphone suppository, and opium-belladonna suppository
  - lidocaine 4% solution, lidocaine 4% cream, hydrocortisone-pramoxine lotion, ointment and cream, and capsaicin 0.035% cream
  - suzetrigine with maintenance of current quantity limits (no PA for the first 2 days/5 tablets).
  - all other oral pain formulations containing acetaminophen or aspirin

Summary of Prior Reviews and Current Oregon Health Plan (OHP) Fee-for-service (FFS) Policy:

- Muscle relaxants:
  - Previous reviews did not show differences in the clinical efficacy between skeletal muscle relaxants for musculoskeletal conditions.
  - Evidence is insufficient to draw firm conclusions regarding the comparative effectiveness between baclofen, tizanidine or dantrolene for spasticity.
  - The skeletal muscle relaxants tizanidine, cyclobenzaprine, and baclofen are more efficacious than placebo for short-term (5 to 7 days) pain relief of acute low back pain.
  - Dantrolene and chlorzoxazone are associated with rare serious dose-related hepatotoxicity.
  - There is no evidence to support using baclofen for alcohol use disorder (AUD) based on a high-quality systematic review and meta-analysis.
  - Non-preferred muscle relaxants require PA every 3 months because of insufficient evidence for long-term use. The use of carisoprodol is limited to an equivalent of a two-week supply (56 tablets), which is consistent with prescribing information, every 90 days. Prior authorization criteria are also in place to prevent the use of carisoprodol with opioids due to safety concerns.
- NSAIDs:
  - Compared to placebo, there is evidence that NSAIDs improve chronic pain and function in people with osteoarthritis (OA) and inflammatory arthritis (e.g., rheumatoid arthritis). In acute and chronic low back pain, NSAIDs improve pain compared to placebo, but differences are small and unlikely to be clinically meaningful. Multiple organizations including American College of Physicians (ACP), VA/DOD, and NICE recommend use of NSAIDs for low back pain.

- There is evidence of no differences in efficacy between specific NSAIDs when treating low back pain or ankylosing spondylitis. In patients with acute soft tissue injuries, there is no clinically meaningful difference in efficacy between NSAIDs and acetaminophen or NSAIDs and opioids, based on moderate to high quality of evidence.
- There are PA criteria for non-preferred products and for ketorolac use beyond 5 days.

- Opioids:
  - Evidence supports modest improvements in pain and function with use of opioids for acute pain or chronic non-cancer pain compared to placebo (high-quality evidence). No difference in pain or functional status has been consistently observed between opioids and non-opioid analgesics for chronic non-cancer pain (low to moderate quality evidence).
  - There is moderate quality from direct and indirect evidence that buprenorphine provides similar reduction in pain intensity with short-term use (less than 6 months) compared to other opioids and low quality evidence that buprenorphine is not safer than other opioids for treatment of chronic pain.
  - Evidence is limited by short follow-up and exclusion of patients at high risk for adverse events, such as opioid overdose and death. Current high-quality guidelines recommend opioid therapy be reserved for patients with proven medical necessity and those who have failed non-opioid analgesic therapy. Chronic opioid therapy should only be considered with documented improvement in pain and function, thorough assessment of risks and benefits of therapy, and with appropriate ongoing monitoring.
  - PA criteria limit short-acting opioid prescriptions to 7 days and no more than 90 milligram morphine equivalents (MME) per day. Quantity limits allow up to 2 prescriptions every 90 days without PA. All prescriptions for long-acting opioids require PA. For authorization of chronic opioid therapy, providers are required to document sustained improvement from treatment, review the prescription drug monitoring program (PDMP) to verify appropriate prescribing patterns, conduct a recent urine drug screen to assess use of illicit drugs, and assess risk of concurrent central nervous system depressants.
- Topical pain medications:
  - Compared to placebo, evidence shows topical NSAIDs improve acute and chronic musculoskeletal pain, but do not differ in efficacy compared to oral NSAIDs for pain related to knee osteoarthritis (low quality evidence). Topical capsaicin (8%) improves postherpetic neuralgia and human immunodeficiency virus (HIV)-neuropathy, but not diabetic peripheral neuropathy compared to low dose capsaicin (0.04%) or placebo. There is insufficient evidence for topical salicylate, low-concentration (0.04%) capsaicin, and topical lidocaine in acute or chronic pain conditions.
  - The 2019 American College of Rheumatology/Arthritis Foundation strongly recommends topical NSAIDs for knee OA and conditionally recommends topical NSAIDs for hand OA. Topical low-concentration (0.04%) capsaicin is conditionally recommended for patients with knee OA and conditionally recommended against use in patients with hand OA.
  - PA is required for non-preferred products. Lidocaine patches are limited to evidence-supported indications and quantities.
- Suzetrigine:
  - Compared to placebo, suzetrigine, a new oral sodium channel blocker, improves pain intensity from 0 to 48 hours after bunionectomy and abdominoplasty (moderate certainty evidence).[20]
  - There is moderate certainty evidence that suzetrigine is not superior to low dose hydrocodone 5 mg/acetaminophen 325 mg given every 6 hours after bunionectomy or abdominoplasty as evaluated by the time-weighted sum of the pain intensity between hours 0 and 48 (SPID48) on the numeric pain rating scale.[20]
  - There is moderate quality evidence that suzetrigine is safe for use for 48 hours, and insufficient evidence based on one open-label, single arm study that suzetrigine is safe for use up to 14 days (mean 9.8 days).[20]

- Suzetrigine is available without PA for up to 48 hours, and covered with prior authorization for up to 14 days for acute pain management. Use of an opioid is not required for authorization of suzetrigine.

Background:
Pain is a common condition that is associated with significant impacts on quality of life, lost work productivity, and healthcare costs. Pain can be classified as acute (generally defined as less than 1 month in duration), subacute (1-3 months in duration), or chronic (>3 months in duration).[21] Acute and subacute pain is generally caused by an injury or response to an underlying disease process. Treatment and management of underlying conditions, when identified, are essential for pain management. Chronic pain can be further classified as secondary chronic pain (based on an underlying medical condition or injury) or primary chronic pain if it is pain is unrelated to a known cause. Untreated acute pain can evolve into chronic pain, and both primary and secondary chronic pain can coexist. Because pain is a clinically complex condition influenced by a wide range of biological, psychological and social factors, treatments for pain also cover a broad range of non-pharmacologic and pharmacologic interventions.

Choice of medication treatment options can depend on treatment setting (inpatient or outpatient), underlying cause or type of pain, duration of pain, risk for adverse events, and individual patient factors. Examples of outpatient medications used for pain management include NSAIDs, acetaminophen, antidepressants (e.g., SNRIs, TCAs), antiepileptics (e.g., gabapentin, pregabalin, carbamazepine), opioids, muscle relaxants, topical pain medications (e.g., capsaicin, lidocaine, NSAIDs), and suzetrigine. Local or regional anesthesia (e.g., anesthetic injections, epidurals, nerve blocks and continuous wound infiltration) is also commonly used for surgical procedures.[22] In 2025, the Oregon legislature passed senate bill 598 which requires the Pharmacy & Therapeutics (P&T) committee, in making recommendations to the Oregon Health Authority, to "ensure there is at least one clinically appropriate non-opioid prescription drug available as an alternative for each opioid prescription drug and ensure the utilization controls and prior authorization requirements are no more restrictive for the non-opioid prescription drug than the utilization controls and prior authorization requirements for the opioid prescription drug". This senate bill defines "clinically appropriate" as use "supported by nationally recognized compendia, clinical guidelines or generally recognized standards of care." Most guidelines for both acute and chronic pain recommend a multimodal approach to pain management.[12,16,18,23] Interventions may include patient education, psychological management, medications, and non-pharmacologic treatments. In acute pain, including pain related to surgeries, this multimodal approach is intended to manage pain, decrease stress responses, reduce reliance on any single agent in order to minimize adverse effects, and assist patients in returning to normal function.[22] In chronic pain, a multimodal approach can help address maladaptive thought processes and comorbid conditions that contribute to pain in order to improve daily function and decrease the impact that pain has on quality of life.[24] Non-pharmacologic treatments for pain management encompass a wide range of physical interventions (such as physical therapy, massage, temperature therapy, exercise, or acupuncture) and psychological interventions (such as cognitive behavioral therapy, mindfulness meditation, acceptance and commitment therapy, or progressive muscle relaxation).[7,12,16,18] Care should include education on sleep, nutrition, stress reduction, mood, exercise, and knowledge of pain.

For the management of chronic pain, current evidence has not demonstrated clinically significant differences in pain or function between classes of analgesics or individual agents. Recommended treatments for chronic primary pain (i.e., pain unrelated to an underlying condition) include antidepressants and non-pharmacotherapy, including physical and psychological interventions.[8,16,18] In people with chronic pain, antidepressants may help with quality of life, pain, sleep and psychological distress, even in the absence of a diagnosis of depression.[12] Certain antiepileptic medications like gabapentinoids (e.g., pregabalin, gabapentin) have evidence of benefit for some specific types of neuropathy such as postherpetic neuralgia and diabetic neuropathy, but mixed evidence of benefit for other types of off-label neuropathic pain.[13,14] Opioids are not routinely recommended for management of chronic non-cancer pain because they are associated with serious long-term harms including increased risk of overdose and development of substance use disorder and have not been associated with clinically significant

improvements in pain intensity or function with long-term use.[16,18,25] Evidence suggests that long-term use of opioids may worsen chronic pain and decrease function compared to treatment with non-opioid medications.[18]

Acute pain management is typically tailored for conditions in which there is evidence of benefit. For example, there is evidence to support NSAIDs for inflammatory conditions like arthritis, gout, tendinitis, pelvic pain, and dysmenorrhea. In post-operative pain, 2016 guidelines from the American Pain Society include recommendations for opioids, acetaminophen, NSAIDs, and gabapentinoids as part of a multimodal approach to pain management.[23] Suzetrigine, a newer non-opioid analgesic approved after publication of these guidelines, also has evidence in acute pain management after surgery.[26] Muscle relaxants have some evidence of benefit with short-term use in patients with low back pain or spasticity, but very limited data on long-term use.[8,17] Similarly, acetaminophen, opioids, and NSAIDs have evidence of benefit in a variety of other acute pain conditions, but also evidence of harms with high doses, long-term therapy, or in people with pre-existing conditions which may increase risk of adverse events. Opioids are associated with risk of dependence, addiction, abuse, misuse, neonatal withdrawal syndrome, overdose, respiratory depression, and death.[16,25] NSAIDs are associated with increased risk of gastrointestinal and cardio-renal adverse events, and acetaminophen has been associated with hepatotoxicity with high doses, concomitant alcohol, or underlying liver disease. For people who are currently on treatments for chronic pain management that have little evidence of benefit, but potential harms, most guidelines recommend an individualized, patient-centered approach to assess benefits, educate patients on risks related to ongoing therapy, and develop strategies for monitoring and risk mitigation if therapy is continued.[12,16,19] When available, interdisciplinary or multidisciplinary care, or multimodal approaches that emphasizes non-pharmacological and self-management strategies are recommended to deprescribe opioids and manage chronic pain.[16,18,19]

In most cases, the goals of pain treatment are to reduce rather than eliminate pain, to improve function, and to reduce the impact pain has on quality of life. Outcomes in clinical trials include assessments of pain intensity (typically via numeric rating scales), physical functioning, emotional functioning, and patient ratings for overall improvement.[18] Validated self-reported questionnaires include the Brief Pain Inventory or Multidimensional Pain Inventory for physical functioning and the Beck Depression Inventory or the Profile of Mood States for emotional functioning.[18] Systematic reviews and guidelines often aggregate data using standardized mean differences (SMD) when pain intensity or functioning has been reported using a variety of rating scales in clinical trials. SMDs of 0.2, 0.5 and 0.8 typically correspond to small, medium and large effect sizes.[27] SMDs less than 0.2 probably represent a clinically insignificant change.[27]

Methods:
A Medline literature search for new systematic reviews and randomized controlled trials (RCTs) assessing clinically relevant outcomes to active controls, or placebo if needed, was conducted. The Medline search strategy used for this review is available in **Appendix 3**, which includes dates, search terms and limits used. The OHSU Drug Effectiveness Review Project, Agency for Healthcare Research and Quality (AHRQ), National Institute for Health and Clinical Excellence (NICE), Department of Veterans Affairs, the Oregon Mental Health Clinical Advisory Group (MHCAG), the Scottish Intercollegiate Guidelines Network (SIGN), and Canada's Drug Agency (CDA-AMA) resources were manually searched for high quality and relevant systematic reviews. When necessary, systematic reviews are critically appraised for quality using the AMSTAR tool and clinical practice guidelines using the AGREE tool. The Food and Drug Administration (FDA) website was searched for new drug approvals, indications, and pertinent safety alerts.

The primary focus of the evidence is on high quality systematic reviews and evidence-based guidelines. Randomized controlled trials will be emphasized if evidence is lacking or insufficient from those preferred sources.

New Systematic Reviews:

A 2024 Cochrane systematic review evaluated efficacy and safety of ibuprofen in acute postoperative pain in children and adolescents under 18 years of age.[1] A literature search through August 2023 identified 43 RCTs (n=4,265) that compared ibuprofen to placebo, acetaminophen, opioids, or other NSAIDs.[1] Studies enrolled between 23 and 741 participants, and only 5 RCTs enrolled participants with a mean age less than 3 years old.[1] Surgeries included both inpatient and ambulatory outpatient surgeries. Ibuprofen was administered orally in 20 of the 23 studies during the preoperative (n=23), intraoperative (n=4), postoperative periods (n=6). Ten RCTs evaluated administration during multiple time periods (n=10).[1] No studies evaluated the prespecified primary outcome of pain relief (≥ 50% improvement in pain intensity). Certainty in the evidence was significantly limited by lack of adequately reported methods and outcomes (37 studies had high or unclear risk of bias in one or more domains).[1]

- Twenty-one studies compared ibuprofen and acetaminophen. Compared to acetaminophen, ibuprofen improved pain intensity by a small amount within 2 hours post-surgery (SMD −0.42, 95% confidence interval [CI] −0.82 to −0.02; 2 RCTs, n=100; moderate-certainty evidence) and at 2 to 24 hours post-surgery (SMD −0.21, 95% CI −0.40 to −0.02; 6 RCTs, n=422 ; low-certainty evidence).[1]
- Two studies evaluated ibuprofen compared to morphine or ketorolac, but did not report outcomes of pain intensity or serious adverse events between groups. Overall adverse events within 7 days of the procedure were less frequent with ibuprofen compared to morphine (relative risk [RR] 0.58, 95% CI 0.40 to 0.83; risk difference [RD] −0.25, 95% CI −0.40 to −0.09; number needed to treat [NNT] 4; 1 RCT, n=154; moderate-certainty evidence) and ketorolac (RR 0.51, 95% CI 0.27 to 0.96; RD −0.29, 95% CI −0.53 to −0.04; NNT 4; 1 RCT, n=59; low certainty evidence).[1]

A 2023 Cochrane systematic review evaluated efficacy and safety of diclofenac in acute postoperative pain in children and adolescents under 18 years of age.[2] The average age of participants ranged from 2.1 to 14.3 years.[2] The review included 32 RCTs (n=2250) that compared diclofenac to placebo (n=3), opioids (n=7), acetaminophen (n=5), bupivacaine (n=5) or other pharmacotherapy (n=10).[2] All surgeries were performed under general anesthesia. The most common types of procedures included tonsillectomies (n=9), strabismus surgeries (n=6); inguinal herniotomies (n=4), appendectomies (n=4), and dental surgeries (n=2).[2] Diclofenac was administered through a variety of routes (rectal, intravenous, ophthalmic, oral, and topical) and was administered preoperatively (n=21), intraoperatively (n=2), and postoperatively (n=9).[2] The prespecified primary outcome was pain relief (≥ 50% improvement in pain intensity); secondary outcomes included pain intensity, adverse events, and serious adverse events.[2] Most studies had high or unclear risk of bias in one or more domains which significantly limited evaluation of evidence and confidence in treatment effects.[2]

- Evidence was graded as very low certainty for pain improvement for all comparisons indicating significant uncertainty in the magnitude of benefit for diclofenac compared to placebo or other analgesic therapy.[2]
- Compared to opioids, there is moderate certainty evidence that diclofenac probably reduces nausea/vomiting (41.0% in opioids, 31.0% in diclofenac; RR 0.75, 95% CI 0.58 to 0.96; 7 RCTs, n=463) and increases risk of any bleeding (5.4% in opioids, 16.5% in diclofenac; RR 3.06, 95% CI 1.31 to 7.13; 2 RCTs, n=222).[2]

A 2021 Cochrane systematic review evaluated perioperative use of NSAIDs during breast surgery.[3] The review identified 12 RCTs (n=1596) which compared NSAIDs to placebo/no treatment (n=8) or an opioid (n=4).[3] NSAIDs included in these studies were diclofenac, ibuprofen, ketorolac, flurbiprofen, parecoxib, and celecoxib. Types of surgeries included breast augmentation surgery, mastectomy, and lumpectomy.[3] Of the studies which compared NSAIDs to opioids, one studied preoperative administration and 4 studied postoperative administration.[3] All except one study had high or unclear risk of bias in one or more domains.[3]

- Compared to placebo, there was low certainty evidence that NSAIDs reduce pain intensity (SMD -0.26, 95% CI -0.49 to -0.03; 3 RCTs, n=310; I^2 = 73%) and opioid use (SMD -0.45, 95% CI -0.85 to -0.05; 4 RCTs, n=304; I^2 = 63%) within 24 hours following surgery.[3] There was little to no difference in the incidence of breast hematomas within 90 days (low certainty evidence) compared to placebo, and evidence for other adverse events was very uncetain.[3]

- Compared to an opioid (e.g., morphine, hydrocodone, hydromorphone, fentanyl), NSAIDs may reduce pain intensity (SMD -0.68, 95% CI -0.97 to -0.39; 3 RCTs, n=200; I^2 = 89%; low-certainty evidence), reduce opioid use (SMD -6.87, 95% CI -10.93 to -2.81; 3 RCTs, n=178; I^2 = 96%; low-certainty evidence), and decrease risk of nausea and vomiting within 24 hours of surgery (RR 0.18, 95% CI 0.06 to 0.57; 3 RCTs, n=128; I^2 = 0%; moderate-certainty evidence).[3] There was little to no difference in the incidence of breast hematomas within 90 days (low certainty evidence) compared to opioids, and evidence for other adverse events was very uncertain.[3]

A 2021 Cochrane systematic evaluating NSAIDs for acute gout identified 28 RCTs (n=3406) compared to placebo, another NSAID, glucocorticoids, or other drug treatment.[4] The average age in the included studies ranged from 44 to 66 years with an average disease duration ranging from 5 to 17 years.[4] Most participants had a single joint affected. Of the 9 trials which enrolled participants regardless of number of joints involved, 66% to 96% had monoarthritis.[4] Included study durations ranged from 4 to 14 days. Most RCTs had unclear or high risk of bias; only 2 RCTs had low risk in all domains.[4]

- Upon comparison of a nonselective NSAID (indomethacin) to a selective COX-2 inhibitor in 6 RCTs (n=1244), there was no difference in pain intensity, inflammation, treatment success (moderate certainty evidence), quality of life, or function (low certainty evidence).[4] The COX-2 inhibitors included celecoxib and other COX-2 inhibitors not available in the US. Indomethacin was associated with increased risk of total adverse events, most commonly gastrointestinal events (mean difference [MD] 21.7%; 95% CI 8.3 to 41.1; number needed to harm [NNH] 5), and withdrawals due to adverse events (MD 3.9%; 95% CI 1% to 9%; NNH 26) compared to selective COX-2 inhibitors (moderate certainty evidence).[4]
- Compared to glucocorticoids (e.g., prednisolone), NSAIDs (e.g., indomethacin or naproxen) did not show a difference in pain intensity, function, treatment success, withdrawals due to adverse events (moderate certainty evidence) or inflammation (low certainty evidence) in short term studies (4-14 days).[4] NSAIDs were probably associated with increased risk of any adverse event compared to glucocorticoids but with significant heterogeneity and imprecision (MD 32.3%; 95% CI 1.6 to 80.8%; NNH 5; 5 RCTs; moderate certainty evidence).[4]

A 2023 Cochrane systematic review evaluated acetaminophen or NSAIDs for pain related to acute otitis media in children.[5] The review included 4 RCTs which compared acetaminophen or ibuprofen to placebo or each other over 1 to 7 days.[5] Of the included studies, 3 RCTs enrolled participants less than 7 years of age.[5] One study prescribed concurrent antibiotics, and another allowed antibiotics at the discretion of the prescribing provider.[5]

- Compared to placebo, pain relief at 48 hours was improved with acetaminophen (children with pain: acetaminophen 10%, placebo 25%; RR 0.38, 95% CI 0.17 to 0.85; NNT 7, low-certainty evidence) and ibuprofen (children with pain: ibuprofen 7%, placebo 25%; RR 0.28, 95% CI 0.11 to 0.70; NNT 6; low-certainty evidence).[5] There was insufficient evidence to evaluate fever and adverse events for both drugs.[5]
- Four RCTs evaluated ibuprofen versus acetaminophen with no differences found between the two treatments for ear pain, mean pain score, fever or adverse events over 1 to 7 days.[5] Evidence was graded as low or very low quality, indicating significant uncertainty in the magnitude of benefit or incidence of adverse events between groups.[5]
- Two trials compared the combination of ibuprofen and acetaminophen to acetaminophen alone, but evidence was limited by small study sizes and imprecise estimates leading to substantial uncertainty in treatment effects (very low certainty evidence).[5]

A 2022 Cochrane systematic review evaluated oxycodone compared to alternative analgesics for cancer-related pain.[9] The review included 42 studies (n=4485) with an average age for enrolled participants ranging from 45 to 75 years.[9] Length of treatment ranged from a single dose to 12 months, and most trials enrolled participants with a variety of cancer types.[9]

- Most included RCTs (n=24) compared controlled-release formulations of oxycodone and morphine.[9] There was no difference between groups in the number of participants who achieved significant pain relief (low certainty evidence). There was low certainty evidence that controlled-release morphine

may have a small, but clinically insignificant, improvement in pain intensity compared to controlled-release oxycodone (difference 0.27 points on a 0-10 point scale; SMD 0.14, 95% CI 0.01 to 0.27; n = 882; 7 RCTs; n=882).[9] These differences were not apparent following sensitivity analyses and exclusion of studies published in Chinese that had unclear risk of bias from lack of reported methods.[9] There was no difference in drowsiness/sedation or nausea between oxycodone and morphine (low certainty evidence) and estimates of effect for other adverse events were very uncertain.[9]
- The review included RCTs that directly compared many other types and formulations of opioids, but evidence was graded as very low certainty for all comparisons and outcomes indicating significant uncertainty in the magnitude of benefit or incidence of adverse events between different opioids.[9]

A 2021 Cochrane systematic review evaluated hydromorphone for cancer-related pain and identified 8 RCTs which compared hydromorphone to other analgesics, including oxycodone, morphine, and fentanyl.[10] There was no clear difference in pain intensity between hydromorphone and other analgesics.[10] Evidence for all efficacy and safety outcomes was graded as very low quality indicating significant uncertainty in the magnitude of benefit or incidence of adverse events between groups.[10]

After review, 37 systematic reviews were excluded due to poor quality (e.g, indirect network meta-analyses or failure to meet AMSTAR criteria), wrong study design of included trials (e.g., observational), comparator (e.g., no control or placebo-controlled), or outcome studied (e.g., non-clinical). Systematic reviews that were used for the development of one of the high-quality guidelines described below are not described separately.

New Guidelines:

Chronic Pain:

In 2021, NICE published recommendations for chronic primary pain management defined as pain that persists for more than 3 months and has no underlying condition that adequately accounts for the pain.[12] Chronic primary pain and chronic secondary pain (due to an underlying condition) can coexist. Pharmacologic treatment recommendations for chronic primary pain include:

- Consider an antidepressant (specifically amitriptyline, citalopram, duloxetine, fluoxetine, paroxetine or sertraline) for people over 18 years of age or people 16 to 17 years of age with specialist consultation.[12] These medicines may help with quality of life, pain, sleep and psychological distress, even in the absence of a diagnosis of depression.
- Do not initiate the following medicines for chronic primary pain in adults as these medications have not consistently demonstrated benefit for chronic primary pain and may be associated with harms: antiepileptics including gabapentinoids, antipsychotics, benzodiazepines, corticosteroid trigger point injections, ketamine, local anesthetics (topical or intravenous), local anesthetic/corticosteroid combination trigger point injections, NSAIDs, opioids, or acetaminophen.[12]
- For people with chronic primary pain already taking one of the medicines listed above that lack evidence of effectiveness, providers should review prescribing as part of shared decision making to educate patients on lack of evidence in chronic primary pain, develop a shared plan for continued safe prescribing if individual benefits outweigh harms, or encourage and support the patient to reduce or stop the medicine when possible if there is little benefit or significant harm.

In 2025, SIGN issued guidance on management of chronic pain (also defined as pain lasting longer than 3 months).[18] Part 1 of this guideline covers recommendations for opioids, naloxone, antidepressants, medicinal cannabis, pain management programs, psychological interventions, self-help interventions and occupation-based interventions. Recommendations for muscle relaxants, simple analgesics, topical analgesics, anti-epileptics, combination therapies will be subsequently published in Part 2 of the guideline. Recommendations were supported by multiple high-quality systematic reviews.

Recommendations for non-pharmacologic therapy include:[18]

- Following appropriate assessment, consider comprehensive pain management programs for people with chronic pain. Pain management programs are comprised of multiple interventions delivered concurrently (typically in a group setting over several sessions or weeks) including psychological interventions (e.g., cognitive behavioral therapy, talk therapy), medication review, pain education, and exercise or physical activity.
- Offer cognitive behavioral therapy (either face-to-face or remotely) for adults with chronic pain.
- Consider face-to-face acceptance and commitment therapy for chronic pain when there is a preference for an acceptance approach.
- Consider mindfulness-based stress reduction for chronic pain when there is a preference for mindfulness approach.
- Consider peer support interventions or digital self-management interventions as part of the holistic and individualized management for people with chronic musculoskeletal pain.

Table 1 describes medication recommendations for opioids, naloxone and antidepressants for chronic pain.

Table 1. SIGN recommendations for use of medications in chronic pain[18]

Recommendations	Supporting Evidence
Opioids	
- Do not routinely consider opioids for people with chronic non-malignant pain. - Short-term use of opioids (up to 3 months) may be prescribed only when other therapies have been fully explored and if potential benefits outweigh risks of serious harms. - When opioids are prescribed, re-assess benefits and risks early and frequently. Adjust dose and discontinue treatment if clinically indicated. - Regularly review opioid doses over 50 MME/day (at least annually and preferably more often) to detect emerging harms or efficacy. - Consultation or review by a pain specialist should be performed when doses exceed 90 MME/day.	- Several high-quality systematic reviews have consistently found either no benefit with opioids in pain severity or function, or only small reductions in pain severity that do not meet thresholds for clinical efficacy, compared to placebo in short-term trials over 1 to 6 months duration (high certainty evidence). - When evaluating only 3- to 6-month trials, no difference in pain intensity or pain response between opioids and placebo are found. Evidence from observational studies suggest that pain-related and functional outcomes may be worse with long-term opioid use (>12 months) compared to not taking opioids. - High-quality network meta-analyses using direct and indirect evidence suggest individual opioids are similarly ineffective (low to very low certainty evidence). - There are insufficient data to draw conclusions about efficacy in different chronic pain conditions. - There was no difference in pain reduction, pain response, or function with opioids vs. non-opioids (e.g., NSAIDs, antiepileptics, antidepressants) in studies evaluating 1 to less than 6 months of treatment (moderate to high certainty evidence). Only one trial (n=231) longer than 12 months evaluated opioids vs. non-opioids, with larger reduction in pain severity with opioids vs. non-opioids. Differences were small (0.5 points on a 10-point scale) and did not meet thresholds for clinical significance. - Opioids increase risk of treatment discontinuation due to adverse events compared to both placebo and non-opioid medication. Common opioid-related adverse events included nausea, vomiting, constipation, somnolence, dizziness, and pruritus. - Observational studies also document an association between opioid use and fractures, falls, and adverse cardiovascular- and endocrine-related outcomes. Increasing opioid dose and duration of use are associated with increasing risk of overdose, opioid-related mortality, injury related to car accidents, and OUD. - While UDS, PDMP use and pill counts can identify current OUD or misuse, there is no reliable evidence that these monitoring methods will *predict subsequent* OUD or misuse. There are available screening tools to assess risk of

	OUD, but limited evidence on effectiveness at predicting future OUD. Measurable treatment goals should be established prior to starting treatment for chronic pain with a strategy for deprescribing if goals are not met.
Naloxone	
- Consider naloxone for people with chronic pain who are prescribed opioids and who may be at risk of an opioid overdose	- Observational studies suggest that co-prescribing naloxone with opioids is associated with 6% fewer opioid-related ED visits with each additional month since the receipt of a naloxone prescription over a one year follow-up period.
Antidepressants	
- Consider duloxetine in people with chronic pain	- Duloxetine has moderate short-term effects on pain reduction and improved physical functioning (low to moderate certainty evidence). Doses above 60 mg per day probably provide no more benefits than standard doses of 60 mg daily. - Milnacipran may reduce pain by a small amount compared to placebo (low to moderate certainty evidence). - There are no head-to-head comparisons of antidepressants for treatment of chronic pain and insufficient data to draw conclusions regarding other antidepressants. Studies of antidepressants evaluated pain improvement over 2 weeks to 9 months, and there are no clinical studies to evaluate long-term pain improvement with antidepressants. - Adverse effects are more common with antidepressants compared to placebo, and data on adverse events reported in clinical trials of people with chronic pain are limited by short study durations, poor outcome reporting, and wide confidence intervals.
Abbreviations: ED = emergency department; mg = milligrams; MME = morphine milligram equivalent; OUD = opioid use disorder; PDMP = prescription drug monitoring program; UDS = urine drug screen.	

In 2022, the VA/DOD updated recommendations on use of opioids for people with chronic pain (**Table 2).**[16]

Table 2. VA/DOD recommendations for opioid use in chronic pain[16]

Topic	**Recommendation**	**Strength of Recommendation**
Initiation and Continuation	Recommend against initiation of opioid therapy for chronic non-cancer pain.	Strong against
	Recommend against long-term opioid therapy, particularly for: - younger age groups, as age is inversely associated with the risk of opioid use disorder and overdose - patients with chronic pain who have a substance use disorder.	Strong against
	For people with opioid use disorder (OUD) and co-occurring chronic pain, there is insufficient evidence to recommend any specific treatment over another between methadone, buprenorphine, or extended-release naltrexone injection.	Neither for nor against
	Buprenorphine is recommended over full opioid agonists for people who need daily opioids for chronic pain, due to lower risk of overdose and misuse.	Weak for

	- The systematic literature review supporting this recommendation found low quality evidence that transdermal buprenorphine was equally effective at controlling pain compared to other opioids and insufficient evidence evaluating safety of buprenorphine compared to other opioids.	
	Recommend against the concurrent use of benzodiazepines and opioids for chronic pain.	Strong against
Dose and Duration	If opioids prescribed, recommend: - Lowest dose and shortest duration as indicated by patient-specific risks and benefits. - Re-evaluation of patient-specific risks and benefits (including monitoring for adverse events, OUD, and risk of overdose) when considering a dose increase. - Re-evaluation at 30 days or fewer after initiating opioid therapy with frequent follow-up visits if opioids are continued. - Against prescribing long-acting opioids for acute pain, as an as-needed medication, or when initiating long-term opioid therapy.	Strong for Strong against
Tapering	There is insufficient evidence to recommend for or against any specific tapering strategies.	Neither for nor against
	A collaborative, patient-centered approach to opioid tapering is recommended.	Weak for
Monitoring	If opioids prescribed, routine assessment and reassessment for suicide risk and self-directed violence is recommended because studies have consistently shown chronic pain is associated with increased risk of suicide.	Strong for
	Assessment for behavioral health conditions, history of traumatic brain injury, and psychologic factors (e.g., negative affect, pain catastrophizing) is recommended when considering long-term opioids; and Recommend screening for these conditions when considering opioids for acute pain as these conditions are associated with higher risk of harm with opioids.	Strong for (chronic pain) Weak for (acute pain)
	If opioids prescribed, ongoing periodic reevaluation of benefits and harms based on individual risk factors is recommended. - Factors considered for this recommendation included evaluation of current standards of care based on the known risks of opioids, lack of studies to directly describe specific reassessment intervals that can improve opioid-related harms, and patient and provider burden for periodic reassessment.	Weak for
Risk Mitigation	Risk mitigation strategies recommended for people prescribed opioids: - Urine drug screening for people on long-term opioids. - Interdisciplinary care to address pain and/or behavioral health problems for people with high risk and/or aberrant behavior. - Pre-operative education to decrease the risk of prolonged opioid use for post-surgical pain.	Weak for

Prior to prescribing opioids for chronic pain, the following should be considered:[16]

- Risks do not outweigh potential functional benefits.
- Patient has a condition that is:
    - Causing severe chronic pain;
    - Interfering with function and quality of life; and

    - Failing to adequately respond to indicated non-pharmacologic and non-opioid pharmacologic therapy. Non-pharmacologic treatments for chronic pain include rehabilitation and manipulative therapies (e.g., physical therapy, occupational therapy, chiropractic medicine), interventional procedures (e.g., trigger point injections, joint injections, acupuncture), psychological and behavioral interventions (e.g., motivational interviewing, cognitive behavioral therapy), and complementary and integrative treatments (e.g., yoga, tai chi).
- Clear and measurable functional goals are established.
- Monitoring:
    - Patient is willing and able to access adequate follow-up for prescribed opioids.
    - PDMP and urine drug screen (UDS) are concordant with expectations (no aberrant behavior)
    - Patient is fully informed and consents to treatment with opioids

For people prescribed opioids, risk mitigation strategies include UDS, PDMP evaluation, overdose education, naloxone distribution, and provider-follow up with frequency determined by risk.[16]

Contraindications for initiation of opioids include evaluation of suicide risk, substance use disorder, and concomitant benzodiazepine use.[16]

In patients already prescribed opioids, evidence of OUD may include self-escalating doses, early refills, difficulty tapering, cravings, continued use despite medical or psychological consequences, and interpersonal or social problems related to opioid use.[16]
Tapering, dose reduction and discontinuation of opioids should be considered when there is:[16]

- Lack of clinically meaningful improvement in functional goals;
- Improvement in the underlying pain condition;
- Pain condition that is not effectively treated with opioids (e.g., back pain with normal MRI; fibromyalgia);
- Increased risk of overdose or adverse events (based on concomitant medications, high dose, or co-occurring medical or behavioral health disorders);
- Lack of participation in risk mitigation measures or comprehensive pain care plan; or
- Significant side effects, overdose, or diversion. Side effects could include risk of developing or worsening opioid use disorder, depression, falls, fractures, sleep disordered breathing, sedation, cognitive dysfunction, motor vehicle accidents, nausea, constipation, dry mouth, hypogonadism, immune system dysfunction, worsening or prolonged pain, and reduction in function or quality of life.

Acute and Chronic Low Back Pain:
In 2022, the VA/DOD updated recommendations for treatment of low back pain.[8] Recommendations included NSAIDs for both acute (<4 weeks) and chronic low back pain and duloxetine for low back pain lasting longer than 4 weeks (weak recommendation for treatment).[8] Recommended non-pharmacologic management included acupuncture, cognitive behavioral therapy and/or mindfulness-based stress reduction, clinician-directed exercise programs, and spinal mobilization/manipulation. They found insufficient evidence to make recommendations for or against gabapentin, pregabalin, tricyclic antidepressants, topical pain medications, or non-benzodiazepine muscle relaxants for short-term use.[8] They suggested against offering muscle relaxants or opioids for chronic low back pain, and against offering acetaminophen, monoclonal antibodies, corticosteroids, or benzodiazepines for people with acute or chronic low back pain.[8]

In 2020, NICE published recommendations for treatment of low back pain and sciatica.[7] Recommendations generally apply when there is not an identified underlying pathology (e.g., cancer, infection, trauma, or inflammatory disease). Recommendations for pharmacologic therapy include use of NSAIDs as an initial treatment option. NSAIDs are recommended at the lowest effective dose for the shortest time with appropriate monitoring and gastroprotective treatment

because of potential risks related to adverse events (including gastrointestinal, liver, cardio-renal toxicity).[7] Codeine with or without acetaminophen can be considered for acute low back pain, only if an NSAID is contraindicated, not tolerated, or ineffective. NICE recommends against routinely offering codeine or other opioids for acute low back pain or for managing for managing chronic sciatica or low back pain lasting more than 3 months. The following therapies are not recommended: gabapentinoids, other antiepileptics, corticosteroids, or benzodiazepines for managing sciatica as there is no evidence of benefit and there is evidence of harm; acetaminophen alone, antidepressants, gabapentinoids, or antiepileptics for low back pain based on a lack of evidence in clinical trials for this specific type of pain. For patients already prescribed gabapentinoids, benzodiazepines, or opioids, discuss with patients about the benefits and harms of these treatments, and safe withdrawal management as part of shared decision-making process.

Chronic Neuropathic Pain:

In 2022, the American Academy of Neurology published treatment guidelines for adults with chronic painful diabetic polyneuropathy (PDN).[14] Recommendations were based on a systematic review and meta-analysis of the evidence evaluating medications by class. Standardized mean differences (SMD) of 0.2, 0.5, and 0.8 were defined for small, medium, and large effect sizes, respectively.[14] In short-term trials over 4-16 weeks, the following medication classes were more likely to improve pain compared to placebo:[14]

- SNRIs (e.g., duloxetine, venlafaxine, and desvenlafaxine): SMD 0.47; 95% CI 0.34 to 0.60; n=1884; 9 trials; moderate confidence evidence
- Gabapentinoids: SMD 0.44; 95% CI 0.25 to 0.63; n= 3,550; 16 trials; moderate confidence evidence
- Sodium channel blocker antiepileptics (e.g., carbamazepine, oxcarbazepine, lamotrigine, valproic acid, lacosamide): SMD 0.56; 95% CI 0.25 to 0.87; n=566; 5 trials; moderate certainty evidence
- SNRI-opioid dual mechanism agents (e.g., tramadol, tapentadol): SMD 0.62; 95% CI 0.38 to 0.86; n= 775; 4 trials; moderate confidence evidence
- Tricyclic antidepressants (e.g., amitriptyline, nortriptyline, imipramine): SMD 0.95; 95% CI 0.15 to 1.75; n=139; 3 trials; low confidence evidence
- Capsaicin: SMD 0.30; 95% CI, 0.14 to 0.47; 2 trials; low confidence evidence

Recommendations for medication therapy include:[14]

- TCAs, SNRIs, gabapentinoids, and/or sodium channel blocker antiepileptics to reduce pain (Level B). Given similar efficacy, clinicians should consider factors other than efficacy, including potential adverse effects, patient comorbidities, cost, and patient preferences, when recommending treatment for PDN (Level B). In patients of childbearing potential with PDN, clinicians should not offer valproic acid (Level B).
- Clinicians may assess patient preferences for effective oral, topical, nontraditional, and nonpharmacologic interventions for PDN (Level C).
- Clinicians should offer patients a trial of a medication from a different effective class when they do not achieve meaningful improvement or if they experience significant adverse effects with the initial therapeutic class (Level B). Adequate trial was defined as titration to a therapeutic dose for about 12 weeks without clinically significant pain reduction or intolerance to side effects. For patients who achieve partial improvement with an initial therapeutic class, clinicians should offer a trial of a medication from a different effective class or combination therapy by adding a medication from a different effective class (Level B).
- Clinicians should not use opioids (Level B) or dual mechanism opioids/SNRI agents (level C) for the treatment of PDN based on limited data on efficacy with long-term use and increased risk of long-term harms. If patients are currently on opioids or dual mechanism opioids/SNRI agents for the treatment of PDN, clinicians may offer the option of a safe taper off these medications and discuss alternative nonopioid treatment strategies (Level C).

In 2020, NICE published recommendations for treatment of neuropathic pain in adults including diabetic neuropathy, post-herpetic neuralgia, trigeminal neuralgia, post-surgical chronic neuropathic pain, and neuropathic cancer pain.[13]

For trigeminal neuralgia, offer carbamazepine as initial treatment.[13] If ineffective, refer to a pain specialist.

For neuropathic pain (except trigeminal neuralgia), medication recommendations include:[13]

- Offer amitriptyline, duloxetine, gabapentin, or pregabalin as initial treatment for neuropathic pain (except trigeminal neuralgia). If initial or subsequent treatment is not effective or tolerated, switch to another of these agents.
- Tramadol may be used only if acute rescue therapy is needed.
- Capsaicin cream may be used for people with localized neuropathic pain who wish to avoid or who cannot tolerate oral treatments.
- Do not start the following therapies for neuropathic pain without consultation from a pain specialist: antiepileptics (e.g., lacosamide, lamotrigine, valproate, levetiracetam, oxcarbazepine, topiramate), capsaicin patch, opioids (e.g., morphine, long-term use of tramadol) or venlafaxine.

Arthritis Pain

In 2022, American Academy of Orthopedic Surgeons published guidelines in adults with knee osteoarthritis.[15] Treatments included both non-pharmacologic and pharmacologic therapy; this summary focuses on medication recommendations. Pharmacologic recommendations were generally consistent with current practice and known evidence (**Table 3**). Recommendations were categorized as strong when there was high quality supporting evidence, moderate when benefits exceed potential harms but evidence is of lower quality, and limited when there is unclear balance between potential benefits and harms.[15]

Table 3. Medication recommendations for adults with knee osteoarthritis[15]

Recommendation	Strength of Recommendation
Topical NSAIDs to improve function and quality of life, when not contraindicated	Strong for
Oral NSAIDs to improve pain and function, when not contraindicated	Strong for
Oral acetaminophen to improve pain and function	Strong for
Opioids, including tramadol, are NOT recommended because they increase adverse events and are not effective at improving pain or function for knee osteoarthritis	Strong against
Intra-articular corticosteroids for short-term pain relief (up to 3 months) for symptomatic osteoarthritis of the knee	Moderate for
Oral supplements including turmeric, ginger extract, glucosamine, chondroitin, and vitamin D to reduce pain and improve function in mild to moderate knee osteoarthritis; however, evidence of efficacy is inconsistent and is very low quality	Limited

Deprescribing opioids

In 2022, the National Health and Medical Research Council of Australia published high-quality guidelines for best practices around opioid deprescribing.[19] In many cases, authors identified insufficient evidence in the literature to support recommendations for deprescribing opioids. Recommendations for which there is available evidence are outlined in **Table 4**.[19] Recommendations were categorized as recommendations that would apply to most or all individuals, conditional recommendations where not all individuals would be served by the recommended action and there need to consider individual patient circumstances, or consensus recommendations based on expert opinion.

Available evidence indicates that patient-prescriber agreements may reduce or mitigate opioid misuse, and there is insufficient evidence to determine if implementation of a deprescribing plan when initiating an opioid reduces opioid-related harms.[19] There is evidence that voluntary deprescribing of opioids does not significantly change pain or function (low certainty evidence), and may improve quality of life (very low certainty evidence).[19] After opioid deprescribing, there were greater improvements in pain intensity for people taking high dose opioids compared to lower dose opioids.[19] Patients who participated in a multidisciplinary or multimodal care model also had greater improvements in pain compared to patients who had less intensive co-interventions.[19] Patients with

less intensive co-interventions were more likely to have pain and function that was unchanged after deprescribing.[19] There is evidence that involuntary deprescribing or tapering may increase risk of substance use, emotional dysregulation, opioid overdose, and suicide.[19] There is insufficient evidence to determine which specific tapering plans are associated with greater success of opioid deprescribing.[19] Many studies did not adequately report tapering approaches, others designed tapering to the individual patient needs, and most studies did not evaluate patients who were unsuccessful completing a taper.[19] The guideline also evaluated evidence of benefits and harms for opioid prescribing and deprescribing in specific populations.

- There is limited evidence to support efficacy and safety of long-term opioid use in cancer survivors (e.g., beyond the acute diagnosis and treatment phase).[19] However, adverse effects have been documented with long-term opioid use including similar rates for opioid misuse when compared to individuals without cancer.[19]
- For people with breathing disorders or who are prescribed concomitant sedating drugs that may increase the risk of opioid-related harms, there is a lack of data for efficacy of opioids, and evidence that opioid prescribing increases risk of opioid-related harms.[19]
- In people nearing the end of life, there is insufficient evidence to evaluate benefits or risk of opioid deprescribing.[19]
- In people with severe opioid use disorders, there is moderate quality evidence that deprescribing alone, without access to long-term substance use disorder treatment and care, is associated with increased risk of overdose and death.[19]

Table 4. Recommendations for Opioid Deprescribing[19]

Recommendation	Classification of Recommendation	Evidence Certainty
We suggest initiating deprescribing for people taking opioids for chronic non-cancer pain if (any of the following): • there is a lack of overall and clinically meaningful improvement from baseline in function, quality of life, or pain; • there is a lack of progress towards meeting agreed therapeutic goals; or • the person is experiencing serious or intolerable opioid-related adverse effects in the physical, psychological or social domains.	Conditional recommendation for (non-cancer pain)	Very low
We suggest avoiding opioid deprescribing for people taking opioids with severe OUD and suggest that evidence-based care, such as transition to, or referral for, medication-assisted treatment of opioid use disorder is provided.	Conditional recommendation against	Moderate
We recommend gradual tapering of opioids. Abrupt cessation of opioids without prior dose reduction may increase risks of harm.	Recommendation for	Low
We recommend tailoring the deprescribing plan based on the person's clinical characteristics, goals, and preferences.	Recommendation for	Very low
When available, we suggest the use of interdisciplinary or multidisciplinary care, or a multimodal approach that emphasizes non-pharmacological and self-management strategies to deprescribe opioids.	Conditional recommendation for	Low
We suggest the consideration of evidence-based co-interventions to support opioid deprescribing.	Conditional recommendation for	Very low

Spasticity and Pain Related to Multiple Sclerosis

In 2022, NICE updated guidelines related to spasticity associated with MS including involuntary muscle movements, muscle stiffness, pain and restriction with certain movement or positions that cause functional impairment, or changes in mobility and upper limb function.[17] Baclofen is recommended as an initial treatment option for people who have spasticity and specific treatment goals such as improving mobility or pain.[17] Prescribers should take into account contraindications, comorbid symptoms, and patient preferences as muscle relaxants may also worsen MS-related symptoms including balance and mobility.[17]

Gabapentin is recommended as a second-line option if baclofen is not tolerated or does not provide adequate relief.[17] Combination therapy with baclofen and gabapentin can be considered if either medication does not provide adequate relief with maximum doses or if adverse effects prevent dose escalation.[17]

After review, 14 guidelines were excluded due to poor quality.

New Formulations or Indications:

New formulations approved by the FDA in the oral muscle relaxants PDL class include:

- Baclofen oral solution (Ozobax DS®), oral suspension (Fleqsuvy®), and oral granules (Lyvispah®) for treatment of spasticity related to multiple sclerosis and in patients with spinal cord injuries.[28-30]
- Cyclobenzaprine orally disintegrating tablets (Tonmya®) for the treatment of fibromyalgia in adults.[31]
- Methocarbamol oral suspension (Atmeksi®) indicated as an adjunct therapy to rest, physical therapy and other measures for the relief of discomfort associated with acute, painful musculoskeletal conditions in patients 16 and older.[32]
- Tizanidine oral solution (Ontralfy™) indicated for treatment of spasticity in adults.[33]

New formulations approved by the FDA in the oral NSAID PDL class include:

- Oxaprozin capsules (Coxanto®) for treatment of osteoarthritis, rheumatoid arthritis, and juvenile rheumatoid arthritis.[34] Oxaproxin was previously available as tablets.
- Celecoxib oral suspension (Vyscoxa®) for treatment of osteoarthritis, rheumatoid arthritis, juvenile rheumatoid arthritis, and ankylosing spondylitis.[35]
- Acetaminophen/ibuprofen 325/97.5 mg oral tablets (Combogesic®) for short-term management of mild to moderate acute pain in adults.[36] Acetaminophen/ibuprofen was previously available in different dosage strengths and forms.

New formulations approved by the FDA in the opioid PDL classes include:

- Tramadol oral solution (Qdolo®) for management of pain in adults that is severe enough to require an opioid analgesic and for which alternative treatments are inadequate.[37]
- Tramadol/celecoxib (Seglentis®) tablets, a new combination product for management of acute pain in adults that is severe enough to require an opioid analgesic and for which alternative treatments are inadequate.[38]

New expanded indications approved by the FDA for any analgesic products include:

- Diclofenac (Zipsor®) capsules for pediatric patients over 12 years of age.[39] Approval was based on studies of evaluating efficacy in adults and pharmacokinetic and safety data in patients 12 to 17 years of age.[39]
- Tapentadol (Nucyenta®) for pediatric patients over 6 years of age who weigh at least 40 kg.[40] Tapentadol was previously approved in adults, and expanded use in pediatric patient was based on a study of 175 patients from 2 to 17 years who underwent surgery expected to cause moderate to severe pain, and were treated with tapentadol oral solution or placebo.[40] Analysis of supplemental opioid use by age showed that patients 6 to 17 years who received placebo had more supplemental opioid analgesic medication used within the 24 hours post-surgery compared to patients prescribed tapentadol.[40] In patients 2 to 6 years of age, supplemental opioid use was numerically greater in the tapentadol group indicating lack of efficacy for very young patients.[40]
- Capsaicin patch (Qutenza®) for treatment of neuropathic pain associated with diabetic peripheral neuropathy of the feet.[41] Capsaicin patch was previously approved for postherpetic neuralgia. Patches are provider administered and applied for 30 minutes to the feet every 3 months for diabetic

peripheral neuropathy.[41] Approval was based on one 12 week, double-blind, placebo controlled, RCT which evaluated pain intensity over 12 weeks. Average pain intensity at baseline was 6.5 (on a 0-10 numeric rating scale), and almost half (47%) of patients were prescribed concomitant treatment with antiepileptics, SNRIs, or TCAs.[41] Pain intensity improved by an average of 1.92 points for people prescribed capsaicin compared to 1.37 points for placebo (LSMD -0.56; 95% CI -0.98 to -0.14) a difference which is unlikely to be clinically significant.[41]

New FDA Safety Alerts:

Table 5. Description of new FDA Safety Alerts.[42]

Generic Name	Brand Name	Month / Year of Change	Location of Change	Addition or Change and Mitigation Principles (if applicable)
NSAIDs	Multiple	April 2021 November 2024	Warnings/Precautions	Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) has been reported in patients taking NSAIDs such as celecoxib. NSAIDs have been associated with serious skin reactions including fixed drug eruption which may present as a more severe variant known as generalized bullous fixed drug eruption.
Opioids	Multiple	December 2023 December 2025	Box Warning Warnings/Precautions	Extensive changes to box warning for various opioids related to risk of addiction, abuse, misuse, and respiratory depression including risk mitigation with naloxone for emergency treatment of opioid overdose. Addition of gabapentinoids as a CNS depressant which may increase risk of sedation, respiratory depression, and death with concomitant opioid use. Risks of gastrointestinal complications: opioid-induced esophageal dysfunction has been reported in patients taking opioids.
Opioids	Multiple	December 2023	Warnings/Precautions	Opioid-Induced Hyperalgesia and Allodynia: opioids can paradoxically cause an increase in pain, or an increase in sensitivity to pain. Carefully consider appropriately decreasing the dose of the current opioid analgesic or opioid rotation (safely switching the patient to a different opioid moiety).
Methadone Tramadol	Methadose® Conzip® Qdolo® Ultram®	December 2023 September 2021	Warnings/precautions	Methadone- and tramadol-associated hypoglycemia have been reported. In most cases, patients had predisposing risk factors such as diabetes; risk may be dose dependent.
Tramadol	Conzip® Qdolo® Ultram®	September 2021	Warnings/precautions	Hyponatremia has been reported with tramadol, and many cases are severe (sodium level <120 mmol/L). Most cases of hyponatremia occurred in females over the age of 65 and within the first week of therapy. In some reports, hyponatremia resulted from the syndrome of inappropriate antidiuretic hormone secretion (SIADH). Monitoring is recommended.

Capsaicin	Qutenza®	July 2024	Warnings/Precautions	Severe Application Site Burns: Cases of full-thickness (third-degree) and deep partial-thickness (second-degree) burns have been reported some of which have required hospitalization and skin grafting in patients who received therapy for unapproved indications and/or frequency of dosing at an application site where there had been prior skin trauma.

Randomized Controlled Trials:

A total of 284 citations were manually reviewed from the initial literature search. After further review, all except 2 citations were excluded because of wrong study design (e.g., observational), setting (e.g., inpatient or single doses in emergency settings), comparator (e.g., no control or placebo-controlled), outcome studied (e.g., non-clinical), or lack of applicability to a US population (e.g. based on intervention or population). Full abstracts are included in **Appendix 2**.

Table 6. Description of Randomized Comparative Clinical Trials.

Study	Comparison	Population	Primary Outcome	Results	Notes/Limitations
Khankhel, et al. 2024.[43] DB, MC, PC, RCT N=198 United States	1. Ibuprofen 400mg + topical placebo gel 2. Diclofenac 1% topical gel + oral placebo 3. Ibuprofen 400 mg + diclofenac 1% topical gel	Adults visiting the emergency department with new onset (within 2 weeks), acute, nontraumatic, nonradicular, musculoskeletal low back pain and functional impairment (RMDQ score >5)	Change in RMDQ (24-point scale evaluating function) after 2 days. A difference of 5 points was predefined as a MCID on the RMDQ.	<u>Change in RMDQ at 2 Days</u> Ibuprofen: 10.0; (95% CI 7.5 to 12.7) Diclofenac: 6.4; (95% CI 4.0 to 8.8) Combination: 8.7 (95% CI 6.3 to 11.1) Ibuprofen vs. diclofenac: MD 3.7 (95% CI 0.2 to 7.2) Ibuprofen vs. Combination: NS Diclofenac vs. Combination: NS <u>Change in RMDQ at 7 days</u> No differences between groups	There were no clinically significant differences in function between people given oral ibuprofen, topical diclofenac, or combination treatment for acute low back pain at 2 or 7 days. Baseline median RMDQ score was 19, 17, and 19 in the 3 groups, respectively. Of the 3083 patients screened, most (n=1837) were excluded because duration of low back pain was > 2 weeks or more frequent than once per month.
Tan, et al. 2026.[6] MC, OL, PG, RCT N=3908 New Zealand	1. APAP 15 mg/kg PO Q6h at age < 1 month and Q4h at age ≥ 1 month 2. Ibuprofen 5 mg/kg PO Q6h at age < 3 months or 10 mg/kg Q6h at age ≥ 3 months	Infants younger than 8 weeks	1. Eczema in the first year of life (defined based on UK diagnostic criteria via parent questionnaire or eczema hospitalization)	Eczema in the first year of life 1. 322 (16.2%) 2. 296 (15.4%) absolute risk difference 0·8% (95% CI –1.5 to 3.1); p=0.48 Bronchiolitis hospitalization in the first year of life 1. 98 (4.9%) 2. 82 (4.3%)	In infants who use ibuprofen or acetaminophen as needed for acute treatment of fever or pain during the first year of life, there is no difference in the incidence of eczema or bronchiolitis at 1 year. Infants were enrolled before 8 weeks of age and parents were supplied with the study drug. Parents completed

	Administered as needed for fever or pain during the first year of life		OR 2. Hospitalization for bronchiolitis (e.g., bronchiolitis, viral-induced wheeze, or asthma) in the first year of life	absolute risk difference 0.7% (95% CI –0.6 to 2.0); p=0.32	questionnaires at 1, 3, 6, 9, and 12 months to report medication use, symptoms, hospital admissions, and exposure to comorbid conditions or confounding environmental factors. Data related to hospitalizations was collected from government health datasets. 97% of infants had at least one dose of acetaminophen; median doses: 16 89% had at least one dose of ibuprofen; median doses: 10

Abbreviations: APAP = acetaminophen; CI = confidence interval; DB = double-blind; h = hours; MC = multicenter; MCID = minimum clinically important difference; MD = mean difference; NS = not significant OL = open label; PC = placebo controlled; PG = parallel group; PO = oral; Q = every; RCT = randomized clinical trial; RMDQ = Roland Morris Disability Questionnaire which is a 24-item scale that evaluates pain-related disability and impact on quality of life; scores range from 0-24 with higher scores indicating more impact on function.

References:

1. Pessano S, Gloeck NR, Tancredi L, et al. Ibuprofen for acute postoperative pain in children. *Cochrane Database of Systematic Reviews.* 2024(1).
2. Ringsten M, Kredo T, Ebrahim S, Hohlfeld A, Bruschettini M. Diclofenac for acute postoperative pain in children. *Cochrane Database of Systematic Reviews.* 2023(12).
3. Klifto KM, Elhelali A, Payne RM, Cooney CM, Manahan MA, Rosson GD. Perioperative systemic nonsteroidal anti-inflammatory drugs (NSAIDs) in women undergoing breast surgery. *Cochrane Database of Systematic Reviews.* 2021(11).
4. van Durme C, Wechalekar MD, Landewé RBM, et al. Non-steroidal anti-inflammatory drugs for acute gout. *Cochrane Database of Systematic Reviews.* 2021(12).
5. de Sévaux JH, Damoiseaux R, van de Pol AC, et al. Paracetamol (acetaminophen) or non-steroidal anti-inflammatory drugs, alone or combined, for pain relief in acute otitis media in children. *Cochrane Database of Systematic Reviews.* 2023(8).
6. Tan E, McKinlay CJD, Riley J, et al. Paracetamol versus ibuprofen as required for fever or pain in the first year of life and the risk of eczema and bronchiolitis at age 1 year in New Zealand (PIPPA Tamariki): a multicentre, open-label, parallel-group, superiority, randomised controlled trial. *The Lancet Child & adolescent health.* 2026;10(3):156-166.
7. National Institute for Health and Care Excellence. Low back pain and sciatica in over 16s: assessment and management. NICE guideline NG59. Updated 11 December 2020. https://www.nice.org.uk/guidance/ng59.
8. VA/DOD Clinical Practice Guidelines. Diagnosis and Treatment of Low Back Pain (LBP) (2022). https://www.healthquality.va.gov/guidelines/Pain/lbp/index.asp. Accessed May 13, 2025.
9. Schmidt-Hansen M, Bennett MI, Arnold S, et al. Oxycodone for cancer-related pain. *Cochrane Database of Systematic Reviews.* 2022(6).

10. Li Y, Ma J, Lu G, et al. Hydromorphone for cancer pain. *Cochrane Database of Systematic Reviews.* 2021(8).
11. Scottish Intercollegiate Guidelines Network. SIGN 136: Management of chronic pain. 2019. Available at: https://www.sign.ac.uk/our-guidelines/management-of-chronic-pain/. Accessed May 13, 2025.
12. Carville S, Constanti M, Kosky N, Stannard C, Wilkinson C. Chronic pain (primary and secondary) in over 16s: summary of NICE guidance. *BMJ (Clinical research ed).* 2021;373:n895.
13. National Institute for Health and Care Excellence. Neuropathic pain in adults: pharmacological management in non-specialist settings. Clinical guideline CG173. Updated 22 September 2020. https://www.nice.org.uk/guidance/cg173.
14. Price R, Smith D, Franklin G, et al. Oral and Topical Treatment of Painful Diabetic Polyneuropathy: Practice Guideline Update Summary: Report of the AAN Guideline Subcommittee. *Neurology.* 2022;98(1):31-43.
15. Brophy RH, Fillingham YA. AAOS Clinical Practice Guideline Summary: Management of Osteoarthritis of the Knee (Nonarthroplasty), Third Edition. *J Am Acad Orthop Surg.* 2022;30(9):e721-e729.
16. VA/DOD Clinical Practice Guidelines. Use of Opioids in the Management of Chronic Pain (2022). https://www.healthquality.va.gov/guidelines/Pain/cot/index.asp. Accessed May 13, 2025.
17. National Institute for Health and Care Excellence. Multiple sclerosis in adults: management. 22 June 2022. https://www.nice.org.uk/guidance/ng220.
18. Scottish Intercollegiate Guidelines Network. SIGN 173 (part 1): Management of chronic pain. 2025. Available at: https://www.sign.ac.uk/guidelines/management-of-chronic-pain/. Accessed February 2, 2026.
19. Langford AV, Schneider CR, Lin CWC, Bero L, Blyth FM, Doctor JN, Holliday S, Jeon YH, Moullin JC, Murnion B, Nielsen S, Osman R, Penm J, Reeve E, Reid S, Wale J, Gnjidic D. Evidence-based Clinical Practice Guideline for Deprescribing Opioid Analgesics. Sydney: The University of Sydney; 2022.
20. Fletcher, S. Drug Use Research and Management. New Drug Evaluation: Suzetrigine (JOURNAVX) 50 mg tablet. April 2025. https://www.orpdl.org/durm/meetings/meetingdocs/2025_06_05/archives/2025_06_05_Journavx_suzetrigine_NDE.pdf. Accessed March 3, 2026.
21. Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC Clinical Practice Guideline for Prescribing Opioids for Pain - United States, 2022. *MMWR Recommendations and reports : Morbidity and mortality weekly report Recommendations and reports.* 2022;71(3):1-95.
22. DynaMed. Management of Acute Perioperative Pain. EBSCO Information Services. Accessed February 10, 2026. https://www.dynamed.com/management/management-of-acute-perioperative-pain.
23. Chou R, Gordon DB, de Leon-Casasola OA, et al. Management of Postoperative Pain: A Clinical Practice Guideline From the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council. *J Pain.* 2016;17(2):131-157.
24. DynaMed. Management of Chronic Pain. EBSCO Information Services. Accessed February 10, 2026. https://www.dynamed.com/management/management-of-chronic-pain.
25. Bavarian R, Sandhu S, Handa S, Shaefer J, Kulich RA, Keith DA. Centers for Disease Control and Prevention Clinical Practice Guideline for Prescribing Opioids: United States, 2022: What dentists need to know. *Journal of the American Dental Association (1939).* 2023;154(9):849-855.
26. Journavx (suzetrigine) tablets [package labeling]. Boston, MA: Vertex Pharmaceuticals. Jan 2026. .
27. Sullivan GM, Feinn R. Using Effect Size-or Why the P Value Is Not Enough. *J Grad Med Educ.* 2012;4(3):279-282.

28. Ozobax DS (baclofen) oral solution. [package labeling]. Athens, GA: Metacel Pharmaceuticals, LLC; September 2023.
29. Fleqsuvy (baclofen) oral suspension. [package labeling]. Woburn, MA: Azurity Pharmaceuticals, Inc.; April 2024.
30. Lyvispah (baclofen) oral granules. [package labeling]. Roswell, GA: Saol Therapeutics, Inc.; November 2021.
31. Tonmya (cyclobenzaprine) tablet, orally disintegrating. [package labeling]. Chatham, NJ: Tonix Medicines, Inc.; October 2025.
32. Atmeksi (methocarbamol) oral suspension. [package labeling]. Watkinsville, GA: Metacel Pharmaceuticals LLC; July 2025.
33. Ontralfy (tizanidine) oral solution. [package labeling]. New Haven, CT: Fidelity BioPharma Co.; December 2024.
34. Coxanto (oxaprozin) capsules. [package labeling]. Madisonville, LA: Solubiomix; November 2024.
35. Vyscoxa (celecoxib) oral suspension. [package labeling]. Hazlet, NJ: Carwin Pharmaceutical Associates, LLC; July 2025.
36. Combogesic (acetaminophen/ibuprofen) tablets, for oral use. [package labeling]. Greenville, NC: Catalent Greenville Inc; November 2024.
37. Qdolo (tramadol hydrocloride) oral solution [package labeling]. Athens, GA: Athena Bioscience, LLC; December 2025.
38. Seglentis (celecoxib/tramadol) tablets, for oral use. [package labeling]. Montgomery, AL: Kowa Pharmaceuticals America, Inc.; November 2024.
39. Zipsor (diclofenac potassium) capsules [package labeling]. Lake Forest, IL: Assertio Therapeutics, Inc; November 2024.
40. Nucynta (tapentadol) tablets [package labeling]. Stoughton, MA: Collegium Pharmaceutical, Inc.; December 2025.
41. Qutenza (capsaicin) topical system [package labeling]. Morristown, NJ: Averitas Pharma, Inc.; July 2024.
42. Food and Drug Administration. Drug Safety-related Labeling Changes (SrLC). https://www.accessdata.fda.gov/scripts/cder/safetylabelingchanges/. Accessed February 15, 2026.
43. Khankhel N, Friedman BW, Baer J, et al. Topical Diclofenac Versus Oral Ibuprofen Versus Diclofenac + Ibuprofen for Emergency Department Patients With Acute Low Back Pain: A Randomized Study. *Annals of emergency medicine.* 2024;83(6):542-551.

Appendix 1: Current Preferred Drug List

Non-steroidal anti-inflammatories, Oral

Generic	Brand	Form	PDL
celecoxib	CELEBREX	CAPSULE	Y
celecoxib	CELECOXIB	CAPSULE	Y
diclofenac potassium	DICLOFENAC POTASSIUM	TABLET	Y
diclofenac sodium	DICLOFENAC SODIUM	TABLET DR	Y
etodolac	ETODOLAC	TABLET	Y
ibuprofen	IBUPROFEN	CAPSULE	Y
ibuprofen	INFANTS' IBUPROFEN	DROPS SUSP	Y
ibuprofen	INFANT'S IBUPROFEN	DROPS SUSP	Y
ibuprofen	CHILDREN'S IBUPROFEN	ORAL SUSP	Y
ibuprofen	IBUPROFEN	ORAL SUSP	Y
ibuprofen	IBUPROFEN	TAB CHEW	Y
ibuprofen	IBUPROFEN IB	TAB CHEW	Y
ibuprofen	IBU	TABLET	Y
ibuprofen	IBU-200	TABLET	Y
ibuprofen	IBUPROFEN	TABLET	Y
ibuprofen	IBUPROFEN IB	TABLET	Y
ibuprofen	IBUPROHM	TABLET	Y
ibuprofen	MOTRIN IB	TABLET	Y
ibuprofen	PAIN RELIEF	TABLET	Y
indomethacin	INDOMETHACIN	CAPSULE	Y
ketoprofen	KETOPROFEN	CAPSULE	Y
meloxicam	MELOXICAM	TABLET	Y
nabumetone	NABUMETONE	TABLET	Y
naproxen	NAPROXEN	TABLET	Y
naproxen	NAPROXEN	TABLET DR	Y
naproxen sodium	ALL DAY PAIN RELIEF	TABLET	Y
naproxen sodium	ALL DAY RELIEF	TABLET	Y
naproxen sodium	NAPROXEN SODIUM	TABLET	Y
oxaprozin	DAYPRO	TABLET	Y
oxaprozin	OXAPROZIN	TABLET	Y
salsalate	SALSALATE	TABLET	Y
sulindac	SULINDAC	TABLET	Y
celecoxib	VYSCOXA	ORAL SUSP	N
diclofenac potassium	DICLOFENAC POTASSIUM	CAPSULE	N
diclofenac potassium	DICLOFENAC POTASSIUM	POWD PACK	N
diclofenac potassium	DICLOFENAC POTASSIUM	TABLET	N
diclofenac potassium	LOFENA	TABLET	N

diclofenac sodium	DICLOFENAC SODIUM ER	TAB ER 24H	N
diclofenac sodium/misoprostol	ARTHROTEC 50	TAB IR DR	N
diclofenac sodium/misoprostol	ARTHROTEC 75	TAB IR DR	N
diclofenac sodium/misoprostol	DICLOFENAC SODIUM-MISOPROSTOL	TAB IR DR	N
diflunisal	DIFLUNISAL	TABLET	N
diflunisal	DOLOBID	TABLET	N
etodolac	ETODOLAC	CAPSULE	N
etodolac	ETODOLAC ER	TAB ER 24H	N
fenoprofen calcium	FENOPROFEN CALCIUM	CAPSULE	N
fenoprofen calcium	NALFON	CAPSULE	N
fenoprofen calcium	FENOPROFEN CALCIUM	TABLET	N
fenoprofen calcium	NALFON	TABLET	N
flurbiprofen	ANSAID	TABLET	N
flurbiprofen	FLURBIPROFEN	TABLET	N
flurbiprofen	LURBIRO	TABLET	N
ibuprofen/famotidine	IBUPROFEN-FAMOTIDINE	TABLET	N
indomethacin	INDOMETHACIN ER	CAPSULE ER	N
indomethacin	INDOMETHACIN	ORAL SUSP	N
ketoprofen	KETOPROFEN	CAP24H PEL	N
ketorolac tromethamine	KETOROLAC TROMETHAMINE	TABLET	N
meclofenamate sodium	MECLOFENAMATE SODIUM	CAPSULE	N
mefenamic acid	MEFENAMIC ACID	CAPSULE	N
meloxicam, submicronized	MELOXICAM	CAPSULE	N
nabumetone	RELAFEN DS	TABLET	N
naproxen	NAPROSYN	ORAL SUSP	N
naproxen	NAPROXEN	ORAL SUSP	N
naproxen sodium	NAPROXEN SODIUM	CAPSULE	N
naproxen sodium	NAPRELAN	TBMP 24HR	N
naproxen sodium	NAPROXEN SODIUM CR	TBMP 24HR	N
naproxen sodium	NAPROXEN SODIUM ER	TBMP 24HR	N
naproxen/esomeprazole mag	NAPROXEN-ESOMEPRAZOLE MAG	TAB IR DR	N
oxaprozin	COXANTO	CAPSULE	N
oxaprozin	OXAPROZIN	CAPSULE	N
piroxicam	PIROXICAM	CAPSULE	N
tolmetin sodium	TOLMETIN SODIUM	CAPSULE	N
tolmetin sodium	TOLECTIN 600	TABLET	N
tolmetin sodium	TOLMETIN SODIUM	TABLET	N
diflunisal	DOLOBID	TABLET	
fenoprofen calcium	FENOPRON	CAPSULE	
ketoprofen	ORUDIS	CAPSULE	

Topical Pain Medications

Generic	Brand	Form	PDL
capsaicin	ARTHRITIS PAIN RELIEVING	CREAM (G)	Y
capsaicin	CAPSAICIN	CREAM (G)	Y
capsaicin	CAPSAICIN-HP	CREAM (G)	Y
diclofenac sodium	ARTHRITIS PAIN	GEL (GRAM)	Y
diclofenac sodium	ARTHRITIS PAIN RELIEVER	GEL (GRAM)	Y
diclofenac sodium	DICLOFENAC SODIUM	GEL (GRAM)	Y
lidocaine HCl	DERMACINRX LIDOCAINE	CREAM (G)	Y
lidocaine HCl	LIDOCAINE HCL	CREAM (G)	Y
lidocaine HCl	GLYDO	JEL/PF APP	Y
lidocaine HCl	LIDOCAINE HCL	JEL/PF APP	Y
lidocaine HCl	LIDOCAINE HCL	SOLUTION	Y
lidocaine HCl	LIDOCAINE HCL	SOLUTION	Y
lidocaine HCl	LIDOCAINE HCL VISCOUS	SOLUTION	Y
lidocaine/prilocaine	LIDOCAINE-PRILOCAINE	CREAM (G)	Y
capsaicin	CAPSAICIN	ADH. PATCH	N
capsaicin	CAPSAICIN HEAT PATCH	ADH. PATCH	N
capsaicin	CAPSIMIDE	ADH. PATCH	N
capsaicin	CAPSAICIN	LOTION	N
capsaicin/me-salicylate/menth	MEDROX	ADH. PATCH	N
capsaicin/me-salicylate/menth	MEDROX	OINT. (G)	N
capsaicin/skin cleanser	QUTENZA	KIT	N
diclofenac epolamine	DICLOFENAC EPOLAMINE	PATCH TD12	N
diclofenac sodium	DICLOFENAC SODIUM	DROPS	N
diclofenac sodium	DICLOFENAC SODIUM	SOL MD PMP	N
diclofenac sodium	PENNSAID	SOLN PK(G)	N
diclofenac/kinesiology tape	LIXOFEN	KIT	N
diclofenac/menthol/camphor	DICLOGEN	KIT	N
hydrocortisone/pramoxine	EPIFOAM	FOAM	N
lidocaine	DERMACINRX LIDOCAN	ADH. PATCH	N
lidocaine	LIDOCAINE	ADH. PATCH	N
lidocaine	LIDOCAN II	ADH. PATCH	N
lidocaine	LIDOCAN III	ADH. PATCH	N
lidocaine	LIDOCAN IV	ADH. PATCH	N
lidocaine	LIDOCAN V	ADH. PATCH	N
lidocaine	LIDODERM	ADH. PATCH	N
lidocaine	TRIDACAINE II	ADH. PATCH	N
lidocaine	TRIDACAINE III	ADH. PATCH	N
lidocaine	TRIDACAINE XL	ADH. PATCH	N

lidocaine	ZTLIDO	ADH. PATCH	N
lidocaine	LIDOCAINE	OINT. (G)	N
lidocaine HCl	LIDAFLEX	ADH. PATCH	N
lidocaine HCl	LIDOTRAL	CREAM (G)	N
lidocaine HCl	DERMACINRX LIDOEASE	GEL (GRAM)	N
lidocaine HCl	DERMACINRX LIDOGEL	GEL (GRAM)	N
lidocaine HCl	DERMACINRX LIDOREX	GEL (GRAM)	N
lidocaine HCl	TRILOGEL	GEL (GRAM)	N
lidocaine HCl	LIDOCAINE HCL	JELLY(ML)	N
lidocaine HCl	DOLOGESIC PAIN RELIEF	LIQD ROLON	N
lidocaine HCl	LIDOCAINE	LIQD ROLON	N
lidocaine/hydrocortisone ac	LIDOCAINE-HYDROCORTISONE	CREAM (G)	N
lidocaine/hydrocortisone ac	LIDOCORT	CREAM (G)	N
lidocaine/kinesiology tape	XYLIDERM	KIT	N
lidocaine/prilocaine	LIDOCAINE-PRILOCAINE	KIT	N
lidocaine HCl	LIDOCAINE HCL	CREAM (G)	
lidocaine HCl	BURN RELIEF	GEL (GRAM)	

Opioids, long-acting

Generic	Brand	Form	PDL
fentanyl	FENTANYL	PATCH TD72	Y
morphine sulfate	MORPHINE SULFATE ER	TABLET ER	Y
morphine sulfate	MS CONTIN	TABLET ER	Y
buprenorphine	BUPRENORPHINE	PATCH TDWK	N
buprenorphine	BUTRANS	PATCH TDWK	N
buprenorphine HCl	BELBUCA	FILM	N
fentanyl	FENTANYL	PATCH TD72	N
hydrocodone bitartrate	HYDROCODONE BITARTRATE ER	CAP ER 12H	N
hydrocodone bitartrate	HYDROCODONE BITARTRATE ER	TAB ER 24H	N
hydrocodone bitartrate	HYSINGLA ER	TAB ER 24H	N
hydromorphone HCl	HYDROMORPHONE ER	TAB ER 24H	N
levorphanol tartrate	LEVORPHANOL TARTRATE	TABLET	N
methadone HCl	METHADONE HCL	ORAL CONC	N
methadone HCl	METHADONE INTENSOL	ORAL CONC	N
methadone HCl	METHADOSE	ORAL CONC	N
methadone HCl	METHADONE HCL	SOLUTION	N
methadone HCl	METHADONE HCL	TABLET	N
methadone HCl	METHADONE HCL	TABLET SOL	N
methadone HCl	METHADOSE	TABLET SOL	N
morphine sulfate	MORPHINE SULFATE ER	CAP ER PEL	N

morphine sulfate	MORPHINE SULFATE ER	CPMP 24HR	N
oxycodone HCl	OXYCODONE HCL ER	TAB ER 12H	N
oxycodone HCl	OXYCONTIN	TAB ER 12H	N
oxymorphone HCl	OXYMORPHONE HCL ER	TAB ER 12H	N
tramadol HCl	CONZIP	CPBP 17-83	N
tramadol HCl	TRAMADOL HCL ER	CPBP 17-83	N
tramadol HCl	CONZIP	CPBP 25-75	N
tramadol HCl	TRAMADOL HCL ER	CPBP 25-75	N
tramadol HCl	TRAMADOL HCL ER	TAB ER 24H	N
tramadol HCl	TRAMADOL HCL ER	TBMP 24HR	N
levorphanol tartrate	XYVONA	TABLET	

Opioids, short-acting

Generic	Brand	Form	PDL
acetaminophen with codeine	ACETAMINOPHEN W/CODEINE	ELIXIR	Y
acetaminophen with codeine	ACETAMINOPHEN-CODEINE	SOLUTION	Y
acetaminophen with codeine	ACETAMINOPHEN W/CODEINE	TABLET	Y
acetaminophen with codeine	ACETAMINOPHEN-CODEINE	TABLET	Y
butorphanol tartrate	BUTORPHANOL TARTRATE	SPRAY	Y
codeine sulfate	CODEINE SULFATE	TABLET	Y
hydrocodone/acetaminophen	HYDROCODONE-ACETAMINOPHEN	SOLUTION	Y
hydrocodone/acetaminophen	HYDROCODONE W/ACETAMINOPHEN	TABLET	Y
hydrocodone/acetaminophen	HYDROCODONE/ACETAMINOPHEN	TABLET	Y
hydrocodone/acetaminophen	HYDROCODONE-ACETAMINOPHEN	TABLET	Y
hydromorphone HCl	HYDROMORPHONE HCL	SUPP.RECT	Y
hydromorphone HCl	DILAUDID	TABLET	Y
hydromorphone HCl	HYDROMORPHONE HCL	TABLET	Y
morphine sulfate	MORPHINE SULFATE	SOLUTION	Y
morphine sulfate	MORPHINE SULFATE	SUPP.RECT	Y
morphine sulfate	MORPHINE SULFATE	TABLET	Y
opium/belladonna alkaloids	BELLADONNA & OPIUM	SUPP.RECT	Y
opium/belladonna alkaloids	BELLADONNA-OPIUM	SUPP.RECT	Y
oxycodone HCl	OXYCODONE HCL	SOLUTION	Y
oxycodone HCl	OXYCODONE HCL	TABLET	Y
oxycodone HCl	ROXICODONE	TABLET	Y
oxycodone HCl/acetaminophen	OXYCODONE W/ACETAMINOPHEN	CAPSULE	Y
oxycodone HCl/acetaminophen	ENDOCET	TABLET	Y
oxycodone HCl/acetaminophen	NALOCET	TABLET	Y
oxycodone HCl/acetaminophen	OXYCODONE HCL-ACETAMINOPHEN	TABLET	Y

oxycodone HCl/acetaminophen	OXYCODONE W/ACETAMINOPHEN	TABLET	Y
oxycodone HCl/acetaminophen	OXYCODONE-ACETAMINOPHEN	TABLET	Y
oxycodone HCl/acetaminophen	PERCOCET	TABLET	Y
tramadol HCl	TRAMADOL HCL	TABLET	Y
acetaminophen/caff/dihydrocod	ACETAMIN-CAFF-DIHYDROCODEINE	CAPSULE	N
aspirin/codeine phosphate	ASPIRIN W/CODEINE	TABLET	N
butalbit/acetamin/caff/codeine	BUTALB-ACETAMINOPH-CAFF-CODEIN	CAPSULE	N
butalbit/acetamin/caff/codeine	FIORICET WITH CODEINE	CAPSULE	N
codeine/butalbital/ASA/caffein	ASA-BUTALB-CAFFEINE-CODEINE	CAPSULE	N
codeine/butalbital/ASA/caffein	ASCOMP WITH CODEINE	CAPSULE	N
fentanyl citrate	FENTANYL CITRATE	LOZENGE HD	N
fentanyl citrate	FENTANYL CITRATE	TABLET EFF	N
hydrocodone/acetaminophen	HYDROCODONE W/ACETAMINOPHEN	ELIXIR	N
hydrocodone/acetaminophen	HYDROCODONE-ACETAMINOPHEN	SOLUTION	N
hydrocodone/acetaminophen	HYDROCODONE-ACETAMINOPHEN	TABLET	N
hydrocodone/acetaminophen	VERDROCET	TABLET	N
hydrocodone/ibuprofen	HYDROCODONE-IBUPROFEN	TABLET	N
hydromorphone HCl	DILAUDID	LIQUID	N
hydromorphone HCl	HYDROMORPHONE HCL	LIQUID	N
meperidine HCl	MEPERIDINE HCL	SOLUTION	N
meperidine HCl	MEPERIDINE HCL	TABLET	N
morphine sulfate	MORPHINE SULFATE	SYRINGE	N
oxycodone HCl	OXYCODONE HCL	CAPSULE	N
oxycodone HCl	OXYCODONE HCL	ORAL CONC	N
oxycodone HCl	ROXYBOND	TABLET ORL	N
oxycodone HCl/acetaminophen	PROLATE	SOLUTION	N
oxycodone HCl/acetaminophen	PROLATE	TABLET	N
oxycodone HCl/acetaminophen	ROXICET	TABLET	N
oxymorphone HCl	NUMORPHAN	SUPP.RECT	N
oxymorphone HCl	OXYMORPHONE HCL	TABLET	N
pentazocine HCl/naloxone HCl	PENTAZOCINE-NALOXONE HCL	TABLET	N
propoxyphene nap/acetaminophen	PROPOXYPHENE NAPSYLATE W/APAP	TABLET	N
tramadol HCl	TRAMADOL HCL	SOLUTION	N
tramadol HCl	TRAMADOL HCL	TABLET	N
tramadol HCl/acetaminophen	TRAMADOL HCL-ACETAMINOPHEN	TABLET	N

Muscle Relaxants, Oral

Generic	Brand	Form	PDL
baclofen	BACLOFEN	TABLET	Y
cyclobenzaprine HCl	CYCLOBENZAPRINE HCL	TABLET	Y

methocarbamol	METHOCARBAMOL	TABLET	Y
tizanidine HCl	TIZANIDINE HCL	TABLET	Y
tizanidine HCl	ZANAFLEX	TABLET	Y
baclofen	LYVISPAH	GRAN PACK	N
baclofen	BACLOFEN	ORAL SUSP	N
baclofen	FLEQSUVY	ORAL SUSP	N
baclofen	BACLOFEN	SOLUTION	N
baclofen	OZOBAX	SOLUTION	N
baclofen	OZOBAX DS	SOLUTION	N
baclofen	BACLOFEN	TABLET	N
carisoprodol	CARISOPRODOL	TABLET	N
carisoprodol	SOMA	TABLET	N
chlorzoxazone	CHLORZOXAZONE	TABLET	N
chlorzoxazone	LORZONE	TABLET	N
cyclobenzaprine HCl	AMRIX	CAP ER 24H	N
cyclobenzaprine HCl	CYCLOBENZAPRINE HCL ER	CAP ER 24H	N
cyclobenzaprine HCl	CYCLOBENZAPRINE HCL	TABLET	N
cyclobenzaprine HCl	FEXMID	TABLET	N
dantrolene sodium	DANTRIUM	CAPSULE	N
dantrolene sodium	DANTROLENE SODIUM	CAPSULE	N
metaxalone	METAXALONE	TABLET	N
methocarbamol	METHOCARBAMOL	TABLET	N
methocarbamol	TANLOR	TABLET	N
orphenadrine citrate	ORPHENADRINE CITRATE ER	TABLET ER	N
orphenadrine/aspirin/caffeine	NORGESIC	TABLET	N
orphenadrine/aspirin/caffeine	NORGESIC FORTE	TABLET	N
orphenadrine/aspirin/caffeine	ORPHENADRINE-ASPIRIN-CAFFEINE	TABLET	N
orphenadrine/aspirin/caffeine	ORPHENGESIC	TABLET	N
orphenadrine/aspirin/caffeine	ORPHENGESIC FORTE	TABLET	N
tizanidine HCl	TIZANIDINE HCL	CAPSULE	N
tizanidine HCl	ZANAFLEX	CAPSULE	N

Appendix 2: Abstracts of Comparative Clinical Trials

Khankhel N, Friedman BW, Baer J, et al. Topical Diclofenac Versus Oral Ibuprofen Versus Diclofenac + Ibuprofen for Emergency Department Patients With Acute Low Back Pain: A Randomized Study. *Annals of emergency medicine*. 2024;83(6):542-551.

STUDY OBJECTIVE: Topical nonsteroidal anti-inflammatory drugs (NSAIDs) are useful for a variety of musculoskeletal injuries. It is not known whether topical NSAIDs should be used for patients presenting with acute nonradicular musculoskeletal low back pain.

METHODS: We conducted a randomized, placebo-controlled double-blind study in which patients 18 to 69 years of age visiting the emergency department (ED) with acute, nontraumatic, nonradicular, musculoskeletal low back pain were randomized at the time of discharge to treatment with 400 mg oral ibuprofen + placebo topical gel, 1% diclofenac topical gel + oral placebo, or 400 mg ibuprofen + 1% diclofenac topical gel. We measured outcomes using the Roland Morris Disability Questionnaire (RMDQ), a 24-item yes/no instrument about the effect of back pain on a respondent's daily activities. The primary outcome was change in RMDQ score between ED discharge and 2 days later. Medication-related adverse events were elicited by asking whether the study medications caused any new symptoms.

RESULTS: In total, 3,281 patients were screened for participation, and 198 were randomized. Overall, 36% of the population were women, the mean age was 40 years (standard deviation, 13), and the median RMDQ score at baseline was 18 (25th to 75th percentile: 13 to 22), indicating substantial low back-related functional impairment. In total, 183 (92%) participants provided primary outcome data. Two days after the ED visit, the ibuprofen + placebo group had improved by 10.1 (95% confidence interval [CI] 7.5 to 12.7), the diclofenac gel + placebo group by 6.4 (95% CI 4.0 to 8.8), and the ibuprofen + diclofenac gel by 8.7 (95% CI 6.3 to 11.1). The between-group differences were as follows: ibuprofen versus diclofenac, 3.7 (95% CI 0.2 to 7.2); ibuprofen versus both medications 1.4 (95% CI -2.1 to 4.9); and diclofenac versus both medications, 2.3 (95% CI -5.7 to 1.0). Medication-related adverse events were reported by 3/60 (5%) ibuprofen patients, 1/63 (2%) diclofenac patients, and 4/64 (6%) patients who received both.

CONCLUSION: Among patients with nontraumatic, nonradicular acute musculoskeletal low back pain discharged from an ED, topical diclofenac was probably less efficacious than oral ibuprofen. It demonstrated no additive benefit when coadministered with oral ibuprofen. Copyright © 2024 American College of Emergency Physicians.

Tan E, McKinlay CJD, Riley J, et al. Paracetamol versus ibuprofen as required for fever or pain in the first year of life and the risk of eczema and bronchiolitis at age 1 year in New Zealand (PIPPA Tamariki): a multicentre, open-label, parallel-group, superiority, randomised controlled trial. *The Lancet Child & adolescent health.* 2026;10(3):156-166.

BACKGROUND: In non-experimental studies, early-life exposure to paracetamol is associated with an increased risk of eczema and wheeze. We aimed to compare paracetamol with ibuprofen, as required for fever or pain in the first year of life, for the risk of eczema and bronchiolitis at age 1 year.,

METHODS: PIPPA Tamariki is a multicentre, open-label, two-arm, parallel-group, superiority, randomised controlled trial done at three sites in Auckland and Wellington in New Zealand. Infants younger than 8 weeks and born in New Zealand were randomly assigned (1:1) to paracetamol alone (15 mg/kg every 6 h at age <1 months and every 4 h at age >=1 months) or ibuprofen alone (5 mg/kg every 6 h at age <3 months and 10 mg/kg every 6 h at age >=3 months), received orally as required for fever or pain, until age 1 year. Dosing was based on the New Zealand Formulary for Children. Research staff used REDCap for randomisation, which was stratified by recruitment site, maternal asthma status, and multiple birth. Key outcomes were eczema as defined by the UK Diagnostic Criteria or eczema hospitalisation in the first year of life, and hospitalisation for bronchiolitis as defined by at least one hospitalisation for bronchiolitis, viral-induced wheeze, or asthma in the first year of life. Analysis was according to the intention-to-treat principle. This trial is registered with the Australian New Zealand Clinical Trials Registry, ACTRN12618000303246 (active, not recruiting).

FINDINGS: Between April 18, 2018, and July 28, 2023, 3923 infants were enrolled. 15 participants withdrew, leaving 3908 infants (1985 were randomly assigned to the paracetamol group, and 1923 to the ibuprofen group) in the intention-to-treat population. Of these participants, 1914 (49.0%) were

female and 1994 (51.0%) were male; 609 (15.6%) were Maori, 607 (15.5%) were Pacific, 926 (23.7%) were Asian, and 1754 (44.9%) were New Zealand European or other. Eczema occurred in 322 (16.2%) of 1985 participants in the paracetamol group and 296 (15.4%) of 1923 participants in the ibuprofen group (absolute risk difference 0.8% [95% CI -1.5 to 3.1]; p=0.48; adjusted odds ratio [OR] 1.10 [95% CI 0.92 to 1.32]; p=0.29). Bronchiolitis occurred in 98 (4.9%) participants in the paracetamol group and 82 (4.3%) participants in the ibuprofen group (absolute risk difference 0.7% [95% CI -0.6 to 2.0]; p=0.32; adjusted OR 1.23 [95% CI 0.82 to 1.71]; p=0.21). 19 serious adverse events were reported in 17 participants (eight [0.4%] of 1985 in the paracetamol group and nine [0.5%] of 1923 in the ibuprofen group; adjusted OR 0.47 [95% CI 0.14-1.56; p=0.21]); none were attributed to trial medication.

INTERPRETATION: There was no evidence of an important difference between paracetamol and ibuprofen in the risk of eczema or bronchiolitis at age 1 year.

FUNDING: Health Research Council of New Zealand, Cure Kids New Zealand, University of Auckland.

Appendix 3: Medline Search Strategy

Ovid MEDLINE(R) ALL 1946 to February 13, 2026

1	exp Analgesics/	626627
2	exp Anti-Inflammatory Agents, Non-Steroidal/	227702
3	exp Narcotics/	155480
4	exp Muscle Relaxants, Central/	45807
5	exp Lidocaine/	27028
6	exp Capsaicin/	11812
7	exp Acetaminophen/	22319
8	suzetrigine.mp.	77
9	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8	690449
10	exp Pain/	498447
11	exp Arthritis/	322907
12	exp Bursitis/	5663
13	exp Tendinopathy/	15760
14	exp Headache Disorders/	43900
15	exp Menstruation Disturbances/	30758
16	exp Neuralgia/	27545
17	exp diabetic neuropathies/ or exp mononeuropathies/ or exp polyneuropathies/	86386
18	exp "Wounds and Injuries"/	1083327
19	exp Muscle Spasticity/	11187
20	exp Fibromyalgia/	11033
21	exp Hiccup/	1270
22	exp Malignant Hyperthermia/	3938
23	10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22	1978731
24	9 and 23	130045
25	limit 24 to (english language and humans and yr="2019 -Current")	23767
26	limit 25 to "systematic review"	1774

27	limit 26 to comparative study	**93**
28	limit 24 to (yr="2021 -Current" and (clinical trial, phase iii or clinical trial, phase iv or randomized controlled trial))	3295
29	limit 28 to comparative study	356
30	exp Administration, Oral/	166224
31	exp Administration, Topical/	102051
32	exp Outpatients/	24094
33	30 or 31 or 32	283391
34	28 and 33	**140**
35	26 and 33	**51**

Appendix 4: Key Inclusion Criteria

Population	People with acute or chronic pain
Intervention	Medications in Appendix 1
Comparator	Medications in Appendix 1
Outcomes	Pain intensity, function, quality of life, disability, need for additional analgesic interventions
Setting	Outpatient

Opioid Analgesics, Short-acting

Goals:

- Restrict use of short-acting opioid analgesics for acute conditions funded by the OHP.
- Encourage appropriate monitoring, risk mitigation, and concomitant therapy for chronic pain.
- Promote use of preferred short-acting opioid analgesics.

Length of Authorization:

- Initial: 7 to 30 days (except 12 months for end-of-life, sickle cell disease, severe burn injury, or cancer-related pain)
- Renewal: Up to 6 months

Covered Alternatives:

- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

Requires a PA:

- Non-preferred short-acting opioids and opioid combination products.
- All short-acting products prescribed for more than 14 days. Each prescription is limited to 7 days in treatment-naïve patients. Patients may fill up to 2 prescriptions every 90 days without prior authorization.
- All codeine and tramadol products for patients under 19 years of age

Note:

- Patients on palliative care with a terminal diagnosis or with cancer-related pain or with pain associated with sickle cell disease or severe burn injury are exempt from this PA.

Table 1. Daily Dose Threshold (90 morphine milligram equivalents per day (MME/day) of Oral Opioid Products.

Opioid	90 MME/day Dose	Notes
Benzhydrocodone	73.5 mg	
Codeine	600 mg	Codeine is not recommended for pediatric use; codeine is a prodrug of morphine and is subject to different rates of metabolism, placing certain populations at risk for overdose.
Dihydrocodeine	360 mg	
Hydrocodone bitartrate	90 mg	
Hydromorphone	22.5 mg	

Levorphanol tartrate	8 mg	
Meperidine	900 mg	Meperidine is not recommended for management of chronic pain due to potential accumulation of toxic metabolites.
Morphine	90 mg	
Oxycodone	60 mg	
Oxymorphone	30 mg	
Tapentadol	225 mg	
Tramadol	400 mg	400 mg/day is max dose and is not equivalent to 90 MME/day. Tramadol is not recommended for pediatric use as it is subject to different rates of metabolism placing certain populations at risk for overdose.

Approval Criteria		
1. What is the patient's diagnosis?	Record ICD10	
2. Has the patient been prescribed any opioid analgesics (short or long-acting) for more than 6 weeks?	**Yes:** Go to **Renewal Criteria**	**No:** Go to #3
3. Is the diagnosis funded by the OHP? Note: Currently, conditions such as fibromyalgia, TMJ, pelvic pain syndrome, neuropathy, and tension headache are not funded by the OHP.	**Yes:** Go to #5	**No:** If not eligible for EPSDT review: Pass to RPh. Deny; not funded by the OHP If eligible for EPSDT review: Go to #4 Note: Management of opioid dependence is funded by the OHP.
4. Is there documentation that the condition is of sufficient severity that it impacts the patient's health (e.g., quality of life, function, growth, development, ability to participate in school, perform activities of daily living, etc)?	**Yes:** Go to #5	**No:** Pass to RPh. Deny; medical necessity.

5. Is the requested medication a preferred agent?	**Yes:** Go to #7	**No:** Go to #6
6. Does the patient have lack of benefit, intolerance, or contraindication to at least 2 preferred product? Note: Preferred opioids are reviewed and designated as preferred agents by the Oregon Pharmacy & Therapeutics Committee based on published medical evidence for safety and efficacy.	**Yes:** Go to #7	**No:** Pass to RPh. Deny; medical appropriateness
7. Is the patient being treated for pain associated with sickle cell disease, severe burn injury or cancer-related pain or under palliative care services with a life-threatening illness or severe advanced illness expected to progress toward dying?	**Yes:** Approve for up to 12 months.	**No:** Go to #8
8. Is the prescription for a product containing codeine or tramadol in a patient less than 19 years of age? Note: Cold symptoms are not funded on the prioritized list	**Yes:** Deny for medical appropriateness	**No:** Go to #9
9. Is the prescription for a short-acting fentanyl product? Note: Short-acting transmucosal fentanyl products are designed for breakthrough cancer pain only. This PA does not apply to transdermal fentanyl patches.	**Yes:** Pass to RPh. Deny; medical appropriateness Note: Management of opioid dependence is funded by the OHP.	**No:** Go to #10

10. Is the opioid prescribed for pain related to migraine or other type of headache? Note: there is limited or insufficient evidence for opioid use for many pain conditions, including migraine or other types of headache.	**Yes:** Pass to RPh. Deny; medical appropriateness	**No:** Go to #11
11. Is the prescriber enrolled in the Oregon Prescription Drug Monitoring Program (www.orpdmp.com) and has the prescriber reviewed at least once in the past 1 month and verified that opioid prescribing is appropriate?	**Yes:** Go to #12	**No:** Pass to RPh. Deny; medical appropriateness.
12. Is the patient currently taking a benzodiazepine or other central nervous system (CNS) depressant? Note: All opioids have a black box warning about the risks of profound sedation, respiratory depression, coma or death associated with concomitant use of opioids with benzodiazepines or other CNS depressants.	**Yes:** Pass to RPh. Deny; medical appropriateness	**No:** Go to #13
13. Within the past 6 weeks, has a 5-day trial of at least one non-opioid analgesic (e.g., NSAID, acetaminophen, and/or muscle relaxant) been tried for this indication at its maximum effective dose and found to be ineffective or are contraindicated?	**Yes:** Go to #14	**No:** Pass to RPh. Deny; medical appropriateness
14. Has the patient already received more than 30 days of opioid therapy for this pain condition?	**Yes:** Go to #15	No: Approve for up to 7 days not to exceed 90 MME

15. Has the prescriber also developed a plan with the patient to stay active (home or prescribed exercise regimen) and with consideration of additional therapies such as behavioral health treatment (e.g., cognitive behavioral therapy), rehabilitative therapy (e.g., physical therapy, yoga, weight loss, massage), or interventional procedures (e.g., spinal manipulation or acupuncture)?	**Yes:** Go to #16	**No:** Pass to RPh. Deny; medical appropriateness
16. Can the prescriber provide documentation of sustained improvement in function of at least 30% compared to baseline with prior use of opioid analgesics (e.g., validated tools to assess function include: Oswestry, Neck Disability Index, SF-MPQ, 3-item PEG scale, and MSPQ)?	**Yes:** Go to #17	**No:** Pass to RPh. Deny; medical appropriateness.
17. Is there a plan to re-evaluate opioid therapy within 30 days?	**Yes:** Approve for up to 30 days	**No:** Pass to RPh. Deny; medical appropriateness.

Renewal Criteria		
1. What is the patient's diagnosis?	Record ICD10 code	
2. Is the request for a patient already established on opioid treatment for >6 weeks (long-term treatment)?	**Yes**: Go to #3	**No**: Go to **Approval Criteria**
3. Does the request document a taper plan for the patient?	**Yes:** Document taper plan and approve for duration of taper or 3 months whichever is less.	**No:** Go to #4

4. Has the patient been referred for alternative non-pharmacologic modalities of pain treatment (e.g., physical therapy, supervised exercise, spinal manipulation, yoga, or acupuncture) AND behavioral health treatment (e.g., cognitive behavioral therapy, acceptance and commitment therapy)?	**Yes:** Go to #5	**No:** Pass to RPh. Deny. Medical appropriateness
5. Is the patient currently prescribed an antidepressant OR is there documentation that the provider has evaluated antidepressant therapy for chronic pain in this patient?	**Yes:** Go to #6	**No:** Pass to RPh. Deny. Medical appropriateness
6. Can the prescriber provide documentation of sustained improvement of at least 30% in pain, function, or quality of life in the past 3 months compared to baseline? Note: Pain control, quality of life, and function can be quickly assessed using the 3-item PEG scale. *	**Yes:** Go to #8 Document tool used and score vs. baseline: _____	**No:** Go to #7
7. Is there documentation that the provider has assessed risks and benefits of tapering opioids within the past 3 months? Assessment should at minimum document 1) evaluation of patient concerns related to tapering, 2) factors which may contribute to increased risk of adverse events and 3) potential for pain improvement with a taper	**Yes:** Go to #8 Document provider attestation and rationale	**No:** Pass to RPh. Deny; medical appropriateness
8. Is the prescriber enrolled in the Oregon Prescription Drug Monitoring Program (www.orpdmp.com) and has the prescriber verified at least once in the past <u>1 month</u> that opioid prescribing is appropriate?	**Yes:** Go to #9	**No:** Pass to RPh. Deny. Medical appropriateness

9. Has the patient had a urinary drug screen (UDS) within the past year to verify absence of illicit drugs and non-prescribed opioids?	**Yes:** Go to #10	**No:** Pass to RPh. Deny. Medical appropriateness
10. Has the member been prescribed or have access to naloxone?	**Yes:** Go to #11	**No:** Pass to RPh. Deny. Medical appropriateness
11. Does the patient have a pain contract on file with the prescriber?	**Yes:** Go to 12	**No:** Pass to RPh. Deny. Medical appropriateness
12. Is the request for an increased cumulative daily dose compared to previously approved therapy or average dose in the past 6 weeks?	**Yes:** Go to #13	**No:** Go to #15
13. Does the total cumulative daily opioid dose exceed 90 MME (see Table 1)?	**Yes:** Pass to RPh. Deny; medical appropriateness	**No:** Go to #14
14. Is there documented rationale (e.g., new acute injury) to support the increase in dose?	**Yes:** Go to #15	**No:** Pass to RPh; deny; medical appropriateness
15. Does the patient have any of the following risk factors for overdose? a. Concomitant CNS depressants (benzodiazepines, muscle relaxants, sedating antipsychotics, etc) b. Total daily opioid dose > 90 MME c. Recent urine drug screen indicating illicit or non-prescribed opioids d. Concurrent short- and long-acting opioid use e. Diagnosis of opioid use disorder	**Yes:** Approved duration is based on the number of identified risk factors for overdose or length of treatment (whichever is less): Risk factors: >=3: 2 month 1-2: 4 months	**No:** Approve for 6 months

*The PEG is freely available to the public http://www.agencymeddirectors.wa.gov/Files/AssessmentTools/1-PEG%203%20item%20pain%20scale.pdf.
Citation of the original publication:
Krebs EE, Lorenz KA, Bair MJ, Damush TA, Wu J, Sutherland JM, Asch SM, Kroenke K. Development and initial validation of the PEG, a 3-item scale assessing pain intensity and interference. *Journal of General Internal Medicine*. 2009 Jun; 24:733-738

Clinical Notes:

How to Discontinue Opioids.

Adapted from the following guidelines on opioid prescribing:

- The Washington State Interagency Guideline on Prescribing Opioids for Pain; Agency Medical Directors' Group, June 2015. Available at http://www.agencymeddirectors.wa.gov/Files/2015AMDGOpioidGuideline.pdf.

Selecting the optimal timing and approach to tapering depends on multiple factors. The decision to taper should be based on shared decision making between the patient and provider based on risks and benefits of therapy. Involving the patient in the decision to taper helps establish trust with the patient, ensures patient-focused tapering, incorporates the patient's values into the taper plan, provides education on the risks of opioid use, and establishes realistic goals and expectations. Avoid insisting on opioid tapering or discontinuation when opioid use may be warranted. The rate of opioid taper should be based primarily on safety considerations, and special attention is needed for patients on high dose opioids or with significant long-term use, as too rapid a taper may precipitate withdrawal symptoms or drug-seeking behavior. In addition, behavioral issues or physical withdrawal symptoms can be a major obstacle during an opioid taper. Patients who feel overwhelmed or desperate may try to convince the provider to abandon the taper. Although there are no methods for preventing behavioral issues during taper, strategies implemented at the beginning of chronic opioid therapy such as setting clear expectations, allowing for pauses during the taper, and development of an exit strategy are most likely to prevent later behavioral problems if a taper becomes necessary.

1. Consider sequential tapers for patients who are on chronic benzodiazepines and opioids. Coordinate care with other prescribers (e.g. psychiatrist) as necessary. In general, taper off opioids first, then the benzodiazepines.
2. Do not use ultra-rapid detoxification or antagonist-induced withdrawal under heavy sedation or anesthesia (e.g. naloxone or naltrexone with propofol, methohexital, ketamine or midazolam).
3. Establish an individualized rate of taper based on safety considerations and patient history. Common tapers have a dose reduction of 5% to 20% per month:
    a. Assess for substance use disorder and transition to appropriate medication assisted treatment if there is diversion or non-medical use,
    b. Rapid taper (over a 2 to 3 week period) if the patient has had a severe adverse outcome such as overdose or substance use disorder, or
    c. Slow taper for patients with no acute safety concerns. May consider starting with a taper of ≤10% of the original dose per month and assess the patient's functional and pain status at each visit.
4. Adjust the rate, intensity, and duration of the taper according to the patient's response (e.g. emergence of opioid withdrawal symptoms (see Table below)).
5. Watch for signs of unmasked mental health disorders (e.g. depression, PTSD, panic disorder) during taper, especially in patients on prolonged or high dose opioids. Consult with specialists to facilitate a safe and effective taper. Use validated tools to assess conditions.
6. Consider the following factors when making a decision to continue, pause or discontinue the taper plan:
    a. Assess the patient behaviors that may be suggestive of a substance use disorder
    b. Address increased pain with use of non-opioid pharmacological and non-pharmacological options.
    c. Evaluate patient for mental health disorders.
    d. If the dose was tapered due to safety risk, once the dose has been lowered to an acceptable level of risk with no addiction behavior(s) present, consider maintaining at the established lower dose if there is a clinically meaningful improvement in function, reduced pain and no serious adverse outcomes.
7. Do not reverse the taper; it must be unidirectional. The rate may be slowed or paused while monitoring for and managing withdrawal symptoms.
8. Increase the taper rate when opioid doses reach a low level (e.g. <15 mg/day MED), since formulations of opioids may not be available to allow smaller decreases.
9. Use non-benzodiazepine adjunctive agents to treat opioid abstinence syndrome (withdrawal) if needed. Unlike benzodiazepine withdrawal, opioid withdrawal symptoms are rarely medically serious, although they may be extremely unpleasant. Symptoms of mild opioid withdrawal may persist for 6 months after opioids have been discontinued (see Table below).
10. Refer to a crisis intervention system if a patient expresses serious suicidal ideation with plan or intent, or transfer to an emergency room where the patient can be closely monitored.

11. Do not start or resume opioids or benzodiazepines once they have been discontinued, as they may trigger drug cravings and a return to use. Counsel the patient on the increased risk of overdose with abrupt return to a previously prescribed higher dose. Provide opioid overdose education and consider offering naloxone.
12. Consider inpatient withdrawal management if the taper is poorly tolerated.

Symptoms and Treatment of Opioid Withdrawal.
Adapted from the Washington State Interagency Guideline on Prescribing Opioids for Pain; Agency Medical Directors' Group, June 2015. Available at http://www.agencymeddirectors.wa.gov/Files/2015AMDGOpioidGuideline.pdf)

Restlessness, sweating or tremors	Clonidine 0.1-0.2 mg orally every 6 hours or transdermal patch 0.1-0.2 mg weekly (If using the patch, oral medication may be needed for the first 72 hours) during taper. Monitor for significant hypotension and anticholinergic side effects.
Nausea	Anti-emetics such as ondansetron or prochlorperazine
Vomiting	Loperamide or anti-spasmodics such as dicyclomine
Muscle pain, neuropathic pain or myoclonus	NSAIDs, gabapentin or muscle relaxants such as cyclobenzaprine, tizanidine or methocarbamol
Insomnia	Sedating antidepressants (e.g. nortriptyline 25 mg at bedtime or mirtazapine 15 mg at bedtime or trazodone 50 mg at bedtime). Do not use benzodiazepines or sedative-hypnotics.

P&T Review: *4/26 (SS); 4/21; 2/20, 9/19, 11/16*
Implementation: *6/1/26; 5/1/21; 3/1/20; 10/1/19; 8/21/17*

Opioid Analgesics, Long-acting

Goals:

- Promote the well-being of OHP members and reduce risk for opioid misuse.
- Provide appropriate opioid coverage for people already prescribed chronic opioid therapy when there is documented sustained improvement in pain and function and routine monitoring for opioid misuse.
- Support appropriate risk mitigation strategies for patients on long-term opioid therapy.
- Promote the safe use of long-acting opioid analgesics by restricting use of high doses that have not demonstrated improved benefit and are associated with greater risk for accidental opioid overdose and death.

Length of Authorization:

- Initial: 90 days (except 12 months for end-of-life, sickle-cell disease, severe burn, or cancer-related pain)
- Renewal: Up to 12 months

Covered Alternatives:

- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

Requires a PA:

- All long-acting opioids and opioid combination products.

Note:

- Patients on palliative care with a terminal diagnosis or with cancer-related pain, or pain associated with sickle cell disease or severe burn injury are exempt from this PA.

Table 1. Daily Dose Threshold (90 Morphine Milligram Equivalents per Day) of Opioid Products.

Opioid	90 MME/day	Notes
Fentanyl (transdermal patch)	37.5 mcg/hr	Use only in opioid-tolerant patients who have been taking ≥60 MME daily for a ≥1 week. Deaths due to a fatal overdose of fentanyl have occurred when pets, children and adults were accidentally exposed to fentanyl transdermal patch. Strict adherence to the recommended handling and disposal instructions is of the utmost importance to prevent accidental exposure.)
Hydrocodone	90 mg	
Hydromorphone	22.5 mg	
Morphine	90 mg	
Oxycodone	60 mg	
Oxymorphone	30 mg	
Tapentadol	225 mg	
Tramadol	300 mg	300 mg/day is max dose and is not equivalent to 90 MME/day. Tramadol is not recommended for pediatric use as it is subject to different rates of metabolism placing certain populations at risk for overdose.
Methadone*	20 mg ***DO NOT USE unless very familiar with the complex pharmacokinetic and pharmacodynamics properties of methadone**. Methadone exhibits a non-linear relationship due to its long half-life and accumulates with chronic dosing. Methadone also has complex interactions with several other drugs. The dose should not be increased more frequently than once every 7 days. Methadone is associated with an increased incidence of prolonged QTc interval, torsades de pointe and sudden cardiac death.	

Table 2. Specific Long-acting Opioid Products Subject to Frequency Limits per FDA-approved Labeling.

Drug Product	Quantity Limit
BELBUCA	2 doses/day
BUTRANS	1 patch/7 days
EMBEDA	2 doses/day
EXALGO	1 dose/day
Fentanyl patch	1 dose/72 hr

Drug Product	Quantity Limit
HYSINGLA ER	1 doses/day
KADIAN	2 doses/day
MORPHABOND	2 doses/day
MS CONTIN	3 doses/day
NUCYNTA ER	2 doses/day

Drug Product	Quantity Limit
OXYCONTIN	2 doses/day
TROXYCA ER	2 doses/day
XARTEMIS XR	4 doses/day
XTAMPZA ER	2 doses/day
ZOHYDRO ER	2 doses/day

		OPANA ER	2 doses/day		

Approval Criteria		
1. What is the patient's diagnosis?	Record ICD10 code	
2. Is the request to initiate a long-acting opioid formulation?	**Yes:** Go to #4	**No:** Go to #3
3. Does the request document a specific taper plan for the patient?	**Yes:** Document taper plan and approve for duration of taper or 3 months whichever is less.	**No:** Go to #4
4. Has the patient failed to have adequate benefit with daily use of short-acting opioids for at least 6 weeks? Note: long-acting opioids are not recommended as initial opioid therapy due to increased risk of death, overdose, and abuse. If trial of an opioid is necessary, short-acting opioids are recommended for initial treatment.	**Yes:** Go to #5	**No:** Pass to RPh. Deny; medical appropriateness. Recommend use of a short-acting product if opioids are necessary
5. Is there documentation that the patient has inadequate response, intolerance, or contraindication to all applicable pharmacologic treatments? Relevant treatments may include: Pharmacologic: topical pain medications, antidepressants, NSAIDs, acetaminophen, or muscle relaxants.	**Yes:** Go to #6	**No:** Pass to RPh. Deny; medical appropriateness.

6. Is there documentation that the treatment will be administered in conjunction with behavioral health therapy (e.g., cognitive behavioral therapy, acceptance and commitment therapy) AND non-pharmacologic modalities of pain management (e.g., physical or occupational therapy, supervised exercise, chiropractic/osteopathic manipulation, interdisciplinary rehabilitation, yoga, or acupuncture)?	**Yes:** Go to #7	**No:** Pass to RPh. Deny; medical appropriateness.
7. Is the patient being treated for pain associated with sickle cell disease, severe burn injury, cancer-related pain or under palliative care services with a life-threatening illness or severe advanced illness expected to progress toward dying?	**Yes:** Approve for up to 12 months	**No:** Go to #8
8. Is the prescriber enrolled in the Oregon Prescription Drug Monitoring Program (www.orpdmp.com) and has the prescriber verified at least once in the past 1 month that opioid prescribing is appropriate?	**Yes:** Go to #9	**No:** Pass to RPh. Deny; medical appropriateness
9. Has the patient had a urinary drug screen (UDS) in the past 1 year and verified absence of illicit drugs and non-prescribed opioids?	**Yes:** Go to #10	**No:** Pass to RPh. Deny. Medical appropriateness
10. Has the member been prescribed or have access to naloxone?	**Yes:** Go to #11	**No:** Pass to RPh. Deny; medical appropriateness.
11. Does the patient have a pain agreement on file with the prescriber?	**Yes:** Go to #12	**No:** Pass to RPh. Deny; medical appropriateness
12. Is the request for an increased cumulative opioid dose compared to previously approved therapy or average dose in the past 6 weeks?	**Yes:** Go to #13	**No:** Go to #16

13. Does the prescription exceed quantity limits applied in Table 2 (if applicable)?	**Yes:** Pass to RPh. Deny; medical appropriateness	**No:** Go to #14
14. Does the total cumulative daily opioid dose exceed 90 MME (see Table 1)?	**Yes:** Pass to RPh. Deny; medical appropriateness	**No:** Go to #15
15. Is there documented rationale (e.g., new acute injury) to support the increase in dose?	**Yes:** Go to #16	**No:** Pass to RPh; deny; medical appropriateness
16. Can the prescriber provide documentation of sustained improvement of at least 30% in pain, function, or quality of life in the past 3 months compared to baseline (e.g., prior to opioid prescribing)? Note: Pain control, quality of life, and function can be quickly assessed using the 3-item PEG scale. **	**Yes:** Go to #17 Document tool used and score vs. baseline: _____	**No:** Go to #18
17. Is the request for a diagnosis for which opioids have not been studied or are not recommended? Examples of conditions for which *long-acting opioids* is are not recommended include fibromyalgia, TMJ, neuropathy, tension headache, migraine, and pelvic pain syndrome	**Yes:** Go to #18	**No:** Go to #19

18. Is there documentation that the provider has assessed risks and benefits of tapering opioids within the past 3 months? Assessment should at minimum document 1) evaluation of patient concerns related to tapering, 2) factors which may contribute to increased risk of adverse events and 3) potential for pain improvement with a taper	**Yes:** Go to #19 Document provider attestation and rationale	**No:** Pass to RPh. Deny; medical appropriateness
19. Does the patient have risk factors for overdose? Risk factors may include, but are not limited to: a. Concomitant CNS depressants (i.e., benzodiazepines, muscle relaxants, sedating antipsychotics, etc.) b. Total daily opioid dose > 90 MME or exceeding quantity limits in Table 2 c. Recent urine drug screen indicating illicit or non-prescribed opioids d. Concurrent short- and long-acting opioid use e. Diagnosis of opioid use disorder f. History of opioid overdose g. Household members, including children, or other close contacts at risk for accidental ingestion or opioid overdose without documentation of secure storage mechanisms (e.g., lockbox, etc)	**Yes:** Go to #20	**No:** Approve for 12 months
20. Has the patient been referred for management of OUD?	**Yes:** Approval for 3 months	**No:** Pass to RPh; deny; medical appropriateness

*See Guideline Note 60 within the Prioritized List of Health Services for conditions of coverage for pain associated with back or spine conditions: http://www.oregon.gov/OHA/HPA/CSI-HERC/Pages/Prioritized-List.aspx

**The PEG is freely available to the public http://www.agencymeddirectors.wa.gov/Files/AssessmentTools/1-PEG%203%20item%20pain%20scale.pdf.
Citation of the original publication:
Krebs EE, Lorenz KA, Bair MJ, Damush TA, Wu J, Sutherland JM, Asch SM, Kroenke K. Development and initial validation of the PEG, a 3-item scale assessing pain intensity and interference. *Journal of General Internal Medicine*. 2009 Jun; 24:733-738.

Clinical Notes:

How to Discontinue Opioids.

Adapted from the following guidelines on opioid prescribing:

- The Washington State Interagency Guideline on Prescribing Opioids for Pain; Agency Medical Directors' Group, June 2015. Available at http://www.agencymeddirectors.wa.gov/Files/2015AMDGOpioidGuideline.pdf.

Selecting the optimal timing and approach to tapering depends on multiple factors. The decision to taper should be based on shared decision making between the patient and provider based on risks and benefits of therapy. Involving the patient in the decision to taper helps establish trust with the patient, ensures patient-focused tapering, incorporates the patient's values into the taper plan, provides education on the risks of opioid use, and establishes realistic goals and expectations. Avoid insisting on opioid tapering or discontinuation when opioid use may be warranted. The rate of opioid taper should be based primarily on safety considerations, and special attention is needed for patients on high dose opioids or with significant long-term use, as too rapid a taper may precipitate withdrawal symptoms or drug-seeking behavior. In addition, behavioral issues or physical withdrawal symptoms can be a major obstacle during an opioid taper. Patients who feel overwhelmed or desperate may try to convince the provider to abandon the taper. Although there are no methods for preventing behavioral issues during taper, strategies implemented at the beginning of chronic opioid therapy such as setting clear expectations, allowing for pauses during the taper, and development of an exit strategy are most likely to prevent later behavioral problems if a taper becomes necessary.

1. Consider sequential tapers for patients who are on chronic benzodiazepines and opioids. Coordinate care with other prescribers (e.g. psychiatrist) as necessary. In general, taper off opioids first, then the benzodiazepines.
2. Do not use ultra-rapid detoxification or antagonist-induced withdrawal under heavy sedation or anesthesia (e.g. naloxone or naltrexone with propofol, methohexital, ketamine or midazolam).
3. Establish an individualized rate of taper based on safety considerations and patient history. Common tapers have a dose reduction of 5% to 20% per month:
    a. Assess for substance use disorder and transition to appropriate medication assisted treatment if there is diversion or non-medical use,
    b. Rapid taper (over a 2 to 3 week period) if the patient has had a severe adverse outcome such as overdose or substance use disorder, or
    c. Slow taper for patients with no acute safety concerns. May consider starting with a taper of ≤10% of the original dose per month and assess the patient's functional and pain status at each visit.
4. Adjust the rate, intensity, and duration of the taper according to the patient's response (e.g. emergence of opioid withdrawal symptoms (see Table below)).
5. Watch for signs of unmasked mental health disorders (e.g. depression, PTSD, panic disorder) during taper, especially in patients on prolonged or high dose opioids. Consult with specialists to facilitate a safe and effective taper. Use validated tools to assess conditions.
6. Consider the following factors when making a decision to continue, pause or discontinue the taper plan:
    a. Assess the patient behaviors that may be suggestive of a substance use disorder
    b. Address increased pain with use of non-opioid pharmacological and non-pharmacological options.
    c. Evaluate patient for mental health disorders.
    d. If the dose was tapered due to safety risk, once the dose has been lowered to an acceptable level of risk with no addiction behavior(s) present, consider maintaining at the established lower dose if there is a clinically meaningful improvement in function, reduced pain and no serious adverse outcomes.
7. Do not reverse the taper; it must be unidirectional. The rate may be slowed or paused while monitoring for and managing withdrawal symptoms.
8. Increase the taper rate when opioid doses reach a low level (e.g. <15 mg/day MED), since formulations of opioids may not be available to allow smaller decreases.

9. Use non-benzodiazepine adjunctive agents to treat opioid abstinence syndrome (withdrawal) if needed. Unlike benzodiazepine withdrawal, opioid withdrawal symptoms are rarely medically serious, although they may be extremely unpleasant. Symptoms of mild opioid withdrawal may persist for 6 months after opioids have been discontinued (see Table below).
10. Refer to a crisis intervention system if a patient expresses serious suicidal ideation with plan or intent, or transfer to an emergency room where the patient can be closely monitored.
11. Do not start or resume opioids or benzodiazepines once they have been discontinued, as they may trigger drug cravings and a return to use. Counsel the patient on the increased risk of overdose with abrupt return to a previously prescribed higher dose. Provide opioid overdose education and consider offering naloxone.
12. Consider inpatient withdrawal management if the taper is poorly tolerated.

Symptoms and Treatment of Opioid Withdrawal.
Adapted from the Washington State Interagency Guideline on Prescribing Opioids for Pain; Agency Medical Directors' Group, June 2015. Available at http://www.agencymeddirectors.wa.gov/Files/2015AMDGOpioidGuideline.pdf)

Restlessness, sweating or tremors	Clonidine 0.1-0.2 mg orally every 6 hours or transdermal patch 0.1-0.2 mg weekly (If using the patch, oral medication may be needed for the first 72 hours) during taper. Monitor for significant hypotension and anticholinergic side effects.
Nausea	Anti-emetics such as ondansetron or prochlorperazine
Vomiting	Loperamide or anti-spasmodics such as dicyclomine
Muscle pain, neuropathic pain or myoclonus	NSAIDs, gabapentin or muscle relaxants such as cyclobenzaprine, tizanidine or methocarbamol
Insomnia	Sedating antidepressants (e.g. nortriptyline 25 mg at bedtime or mirtazapine 15 mg at bedtime or trazodone 50 mg at bedtime). Do not use benzodiazepines or sedative-hypnotics.

P&T Review: *4/26(SS); 2/23; 4/21; 2/20, 9/19, 3/17; 11/16; 05/16*
Implementation: *6/1/26; 4/1/23; 5/1/21; 3/1/20; 10/1/19*

Skeletal Muscle Relaxants

Goal(s):

- Promote use of preferred products
- Cover non-preferred drugs only for short-term treatment or when there is documented evidence of benefit.
- Restrict carisoprodol to short-term use due to lack of long-term studies to assess safety or efficacy and high potential for abuse.

Length of Authorization:

- Up to 3 - 6 months

Requires PA:

- Non-preferred agents

Covered Alternatives:

- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

Approval Criteria		
1. What diagnosis is being treated?	Record ICD10 code	
2. Has the patient had inadequate benefit, intolerance, or contraindication to at least 2 preferred products? Message: • Preferred products do not require PA • Preferred products are evidence-based reviewed for comparative effectiveness and safety by the Pharmacy and Therapeutics (P&T) Committee.	**Yes:** Go to #3	**No:** Pass to RPh; Deny medical appropriateness
3. Has an opioid been prescribed within the past 30 days?	**Yes:** Go to #4	**No:** Go to #5
4. Is there documentation that the opioid will not be prescribed in conjunction with the muscle relaxant OR is there documentation that the provider has implemented a taper and risk mitigation plan for concomitant prescribing? At minimum, a risk mitigation plan should document 1) evaluation of factors contributing to overdose risk, 2) informed consent and patient education on risk of overdose, and 3) concomitant naloxone prescribing.	**Yes:** Go to #5	**No:** Pass to RPh. Deny; medical appropriateness.
5. Is there documentation of symptom impact on function or quality of life using a validated scale?	**Yes:** Go to #6	**No:** Pass to RPh. Deny; medical appropriateness.
6. Is drug requested carisoprodol?	**Yes:** Go to #7	**No:** Go to #10

Approval Criteria		
7. Does total quantity of carisoprodol exceed 56 tablets in 90 days? From claims, document product, dose, directions, and amount used during last 90 days.	**Yes:** Go to #8	**No:** Approve for up to 3 months
8. Does patient have a terminal illness (e.g. metastatic cancer, end stage Parkinson's disease, ALS)?	**Yes:** Approve for 6 months.	**No:** Pass to RPh. Go to #9

9. Pharmacist's statement:
 	
• Carisoprodol cannot be approved for long term usage.
• Patients are limited to 56 tablets in a 90 day period.
• It is recommended that the patient undergo a "taper" of the carisoprodol product of which a supply may be authorized for this to occur.
• The amount and length of taper depends upon the patient's condition. Does the patient meet one or more of the following:
  ○ >65 years of age; or
  ○ renal failure; or
  ○ hepatic failure; or
  ○ take > 1400 mg per day?
	Yes: Document reason and approve long taper:
	
	• Authorize 18 tablets
	• Reduce dose over 9 days
	• 350 mg TID X 3 days, then
	• 350 mg BID X 3 days, then
	• 350 mg daily x 3 days then evaluate
		No: Approve short taper:
		
		• Authorize 10 tablets
		• Reduce dose over 4 days
		• 350 mg TID x 1 day, then
		• 350 mg BID x 2 days, then
		• 350 mg daily x1 day, then evaluate

10. Is the request for acute treatment (<3 months duration) or intermittent use for acute symptoms? Note: Intermittent use may be validated based on claims history.	**Yes:** Approve for up to 3 months	**No:** Go to #11
11. Is the request for continuation of treatment for a patient already established on chronic therapy?	**Yes:** Go to 12	**No:** Approve for up to 3 months

Approval Criteria		
12. Is there documentation of improvement in symptoms, function, or quality of life using a validated scale? The same scale used to evaluate symptoms prior to treatment should be used to assess benefit.	**Yes:** Approve for up to 6 months	**No:** Pass to RPh. Deny; medical appropriateness.

P&T Review: *4/26(SS); 9/19 (KS); 3/17; 11/14; 9/09; 2/06; 2/04; 11/01; 2/01; 9/00; 5/00; 2/00*
Implementation: *6/1/26; 4/1/17; 1/1/15, 1/1/14, 1/1/10, 11/18/04*

Analgesics, Non-Steroidal Anti-Inflammatory Drugs

Goal(s):
- To ensure that non-preferred oral and nasal spray NSAIDs are used for conditions funded by the OHP and support individual review for the EPSDT program.
- Restrict ketorolac to short-term use (5-day supply every 60 days) per the FDA black boxed warning.

Length of Authorization:
- Up to 12 months

Requires PA:
- Non-preferred oral and nasal spray NSAIDs.
- Ketorolac: Maximum of one claim per 60 days, with a maximum 20 tablets/5-day supply or 126 mg/day for nasal spray (maximum 5-day combined duration of treatment every 60 days).

Preferred Alternatives:
- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

Approval Criteria		
1. What diagnosis is being treated?	Record ICD10 code.	
2. Is the diagnosis funded by the Oregon Health Plan?	**Yes:** Go to #4	**No:** If not eligible for EPSDT review: Pass to RPh. Deny; not funded by the OHP If eligible for EPSDT review: Go to #3.
3. Is there documentation of medical appropriateness and medical necessity? Definitions for medical appropriateness include use for an FDA indication AND use, contraindication, or intolerance to preferred agents in the class. Medical necessity includes documentation that the diagnosis impacts the patient's health.	**Yes:** Go to #4	**No:** Pass to RPh; deny medical appropriateness or medical necessity
4. Is this a request for ketorolac, new or continuation of current therapy (i.e. filled prescription within prior 90 days)? Verify via pharmacy claims.	**Yes:** Document prior therapy in PA record. Go to #5.	**No:** Go to #6
5. Is request for more than a 5-day supply of ketorolac within 60 days (200 mg total over 5 days for tablets, 630 mg total over 5 days for the nasal spray)?	**Yes:** Pass to RPh. Deny; medical appropriateness.	**No:** Go to #6

Approval Criteria		
6. Is there documentation that the patient has had inadequate benefit, intolerance, or contraindication to at least 3 preferred products? Message: • Preferred products do not require PA. • Preferred products are evidence-based and reviewed for comparative effectiveness & safety by the Pharmacy and Therapeutics (P&T) Committee.	**Yes:** Approve for requested duration, up to 12 months (whichever is less).	**No:** Pass to RPh. Deny; medical appropriateness.

P&T Review: *4/26 (SS); 12/22; 2/21, 3/16; 11/14; 9/13; 2/12; 9/09; 2/06*
Implementation: *6/1/26; 1/1/23; 1/1/15, 1/1/14, 5/14/12, 1/1/10*

Lidocaine Patch

Goal(s):
- Provide coverage only for diagnoses that are supported by the medical literature.
- Restrict use to OHP-funded diagnoses in adults. Allow case-by-case review for members covered under the EPSDT program.

Length of Authorization:
- 90 days to 12 months (criteria specific)

Requires PA:
- Lidocaine Patch

Covered Alternatives
- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

Approval Criteria	
1. What diagnosis is being treated?	Record ICD10 code

Approval Criteria		
2. Is the diagnosis supported by evidence for its use in that condition (refer to Table 1 for examples)?	**Yes:** Go to #3	**No:** Pass to RPh. Deny; medical appropriateness.
3. Is the diagnosis an OHP-funded diagnosis (refer to Table 1 for examples)?	**Yes:** Go to # 5	**No:** If not eligible for EPSDT review: Pass to RPh. Deny; not funded by the OHP If eligible for EPSDT review: Go to #4.
4. Is there documentation that the condition is of sufficient severity that it impacts the patient's health (e.g., quality of life, function, growth, development, ability to participate in school, perform activities of daily living, etc)?	**Yes:** Approve for 90 days	**No:** Pass to RPh. Deny; medical necessity.
5. Is this a request for renewal of a previously approved prior authorization for lidocaine patch?	**Yes**: Go to **Renewal Criteria**	**No**: Go to #6
6. Is the prescription for Lidoderm patch greater than 3 patches/day?	**Yes:** Pass to RPh. Deny; medical appropriateness	**No:** Approve for 90 days

Renewal Criteria		
1. Does the patient have documented improvement from lidocaine patch?	**Yes:** Approve for up to 12 months	**No:** Pass to RPh. Deny for medical appropriateness.

Table 1. OHP Funded Diagnosis and Evidence Supports Drug Use in Specific Indication

Condition	Lidocaine Patch
Funded	Evidence Supports Use
Diabetic Neuropathy	X

Postherpetic Neuropathy	X
Painful Polyneuropathy	X
Spinal Cord Injury Pain	
Chemotherapy Induced Neuropathy	
Non-funded	
Fibromyalgia	

P&T Review: *4/26 (SS); 8/20 (DM); 7/18; 3/17*
Implementation: *4/1/17*

Suzetrigine (Journavx™)

Goal(s):
- Allow use in accordance with available medical evidence for safety and efficacy.

Length of Authorization:
- Up to 14 days per acute injury/surgery

Requires PA:
Suzetrigine quantities greater than 5 tablets total (50 mg tablets, a 48-hour supply) within 30 days

Covered Alternatives:
- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

Approval Criteria		
1. What diagnosis is being treated?	Record ICD10 code.	
2. Is the patient an adult 18 years or older?	**Yes**: Go to #3	**No:** Pass to RPh. Deny; medical appropriateness.
3. Is the request for treatment of acute pain? Note: Acute pain is generally considered to last less than 30 days.	**Yes**: Go to #4	**No:** Pass to RPh. Deny; medical appropriateness.

Approval Criteria		
4. Is the pain documented to be moderate to severe?	**Yes**: Go to #5 Record pain rating_____ using visual analogue scale (VAS), numeric pain rating scale (NPRS) or other validated measure.	**No:** Pass to RPh. Deny; medical appropriateness.
5. Has the patient already received 14 days of suzetrigine for this indication?	**Yes:** Pass to RPh. Deny; medical appropriateness.	**No:** Go to #6
6. Is there documentation that the patient is failing to receive adequate pain relief from, or have contraindications to, both acetaminophen and a non-steroidal anti-inflammatory agent?	**Yes:** Approved requested doses up to maximum 30 tablets (total includes any doses received before prior authorization requirement).	**No:** Pass to RPh. Deny; medical necessity.

P&T/DUR Review: 4/26(SS); 6/25 (SF)
Implementation: 8/1/25