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Drug Class Literature Scan: Opioids

Date of Review: February 2020

Date of Last Review: September 2019
Literature Search: 04/01/19 – 01/03/20

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

Purpose for Review:
To review current best practice standards for appropriate dosage reduction or discontinuation of chronic opioid therapy. New guidance from United States Department of Health and Human Services (HHS) has been published on appropriate dosage reduction of long-term opioid analgesics and the Oregon Opioid Tapering Task Force has voted to approve clinical guidelines on opioid tapering.

Conclusions:
- One systematic review[1] and one new comparative randomized controlled trial (RCT)[2] was identified. Current evidence supports quantity and dose limits for acute conditions.
- Two new guidelines from HHS and draft guidance from the Oregon Opioid Tapering Task force were available for review.[3,4] Guidelines review best practice standards for opioid tapers in patients with chronic use and include recommendations for an individualized, patient-centered approach for initiation of opioid tapers for patients where risks of opioid use outweigh benefits.

Recommendations:
- Update PA criteria for short- and long-acting opioids to better address patients already established on long-term opioids (**Appendix 6**). The goal of these changes is to prevent harm from abrupt discontinuation of opioids and reinforce a shared patient and provider decision for appropriate dosage reduction.

Summary of Prior Reviews and Current Policy
- Current 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). Compared to other analgesics such as nonsteroidal anti-inflammatory drugs (NSAIDs) or nortriptyline, there is no difference in pain or functional status compared to opioids for chronic non-cancer pain (low to moderate quality evidence). Overall, evidence is limited by short follow-up and exclusion of patients at high risk for adverse events. Current high quality guidelines recommend opioid therapy be reserved for patients who 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.
- Currently FFS prior authorization (PA) criteria limits all 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 a PA. All prescriptions for long-acting opioids require a PA. Prior to implementation

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of this policy, patients already prescribed opioids for chronic use were grandfathered at their current dose to avoid interruptions in care for patients already established on long-term therapy. For authorization of chronic therapy, providers are required to document sustained improvement from treatment, review the PDMP to verify appropriate prescribing, conduct a recent urine drug screen to assess for illicit drugs, and assess risk of concurrent central nervous system depressants.

- In May 2019, HERC guidelines were updated to remove required taper plans for patients using chronic short-acting opioids for back and spine conditions. Language was revised to state: "For patients receiving long-term opioid therapy (>90 days) for conditions of the back and spine, continued coverage of opioid medications requires an individual treatment plan which includes a taper plan *when clinically indicated*." Subsequently, HHS has released guidance for clinicians on appropriate dosage reduction and new guidance has been approved by the Oregon Opioid Tapering Task Force. Recommendations from these organizations are reviewed below.

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. A summary of the clinical trials is available in **Appendix 2** with abstracts presented in **Appendix 3**. The Medline search strategy used for this literature scan is available in **Appendix 4**, 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, and the Canadian Agency for Drugs and Technologies in Health (CADTH) 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 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 Cochrane systematic review evaluated efficacy and safety of tramadol for treatment of osteoarthritis.[1] This summary will focus on the available direct comparative evidence. Only 11 trials were included which compared tramadol to other active treatments.[1] Tramadol doses ranged from 37.5 to 400 mg per day and trials had a mean duration of 2 months.[1] Overall, evidence was limited by unclear risk for selective reporting, allocation concealment and blinding of providers.[1] About half of the included studies had high risk of reporting bias based on incomplete outcome data.[1] There was insufficient evidence to compare efficacy or safety of tramadol to acetaminophen.[1] There was moderate quality evidence that tramadol was slightly less effective than NSAIDs at pain reduction (standardized mean difference [SMD] 0.21, 95% confidence interval [CI] 0.07 to 0.36) and no different compared to other opioids (SMD –0.11, 95% CI –0.33 to 0.12).[1] Upon analysis of tramadol/acetaminophen compared to NSAIDs or opioids, there was no statistical difference in pain reduction. Differences in physical functioning compared to NSAIDs or other opioids were small. Tramadol therapy resulted in slightly worse physical functioning compared to NSAIDs (average worsening of 5 points [95% CI 2 to 8] on a 0 to 100 scale) and slightly better functioning compared to other opioids (67% vs. 51% of patients who defined their treatment as good or better; number needed to treat [NNT] of 7).[1] There was low quality evidence that participants treated with tramadol had a greater risk of withdrawing due to adverse events compared to NSAIDs (21% vs. 11%; relative risk [RR] 1.88, 95% CI 1.27 to 2.76) or other opioids (31% vs. 14%; RR 2.26, 95% CI 1.52 to 3.37).[1]

After review, 8 systematic reviews were excluded due to poor quality,[5] wrong study design of included trials (e.g., observational),[6-8] setting (e.g., inpatient),[9] comparator (e.g., no control or placebo-controlled),[10-13] or outcome studied (e.g., non-clinical).[14]

New Guidelines:
High Quality Guidelines: No new high quality guidelines were identified.

Additional Guidelines for Clinical Context:
HHS Guidelines for appropriate dosage reduction or discontinuation of long-term opioid analgesics were published in October 2019.[3] Methods for the development of this guideline were unavailable and the quality of recommendations could not be assessed. These guidelines emphasize the importance of care coordination and individualized patient care during initiation of an opioid taper plan in order to avoid risks associated with rapid discontinuation.[3] Risks of abrupt or rapid tapers can include withdrawal symptoms, worsening pain, psychological stress/suicidality, seeking opioids from high-risk sources, and loss of patient trust.[3] Required tapering should be avoided, particularly when benefits of opioid therapy continue to outweigh risks. Instead, the decision to taper opioids should be based on a shared decision between the patient and provider.[3] Use of shared decision making when developing tapers helps to 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.[3]

HHS guidelines recommend tapering to a reduced dose or discontinuation of opioid therapy be *considered* in the following circumstances:[3]

- When pain improves
- When pain and function are not meaningfully improved
- Upon receipt of higher doses without documented benefit from higher dose
- When there is evidence of opioid misuse
- With significant adverse effects which affect quality of life or function
- When the patient experiences an overdose or with warning signs for overdose of confusion, sedation or slurred speech
- With co-prescribing of sedating medications or comorbid conditions that increase risk for adverse events
- With long-term prescribing and current risk-benefit assessment is unclear

A variety of tools and methods are recommended to support dosage reduction and include the following:

- Dosage reduction should be individualized based on patient history and goals.[3]
    - Commonly, a dose reduction of 5% to 20% per month is used in practice.
    - Use of slower tapers which may be better tolerated especially in patients with a history of long-term opioid use.
    - Faster tapers may be considered if safety concerns associated with opioid use are identified or with shorter-term use (weeks to months rather than years).
    - Development of flexible taper plans with routine evaluation and options to pause tapering may increase changes of success and decrease patient symptoms.
- Use of supporting therapy and a multidisciplinary treatment approach may improve patient outcomes.[3]
    - Integrate non-pharmacological and non-opioid pharmacological treatments into the therapy plan.
    - Provide behavioral health support and address and treat comorbid mental health conditions.

- Referral to a specialist is recommended if an imminent patient safety concern is identified or for unique populations such as patients with comorbid severe mental illness, other substance use disorders, or pregnancy.
- If there is evidence of misuse guidelines recommend assessment for opioid use disorder with evidence-based medication-assisted treatment when clinically indicated. Consider transition to buprenorphine for patients who are unsuccessful with even slow tapers.
- Manage symptoms of opioid withdrawal by slowing or pausing the taper and adding appropriate symptomatic treatment when indicated
- Reassess plan and symptoms at least quarterly for all patients. Close monitoring is recommended in patients who are unable or unwilling to taper and continue to be prescribed a high-risk regimen.

The Oregon Opioid Tapering Guidelines were approved by the Oregon Opioid Tapering Task Force in October 2019.[4] The methodology for the guideline development was unavailable. A draft of the Oregon guideline was available for review and includes many of the same best practices as outlined in the national HHS recommendations for opioid dose reduction. The goal of these guidelines is to reduce harms associated with opioid use and promote patient-centered care. Recommendations focus on individualized, shared decision making between patients and their provider regarding opioid tapers. Recommendations for health systems include support for a team-based, integrated approach to opioid tapering while ensuring access to multidisciplinary supports, non-opioid pharmacotherapy, and non-pharmacologic treatments.

After review, 1 guideline was excluded due to poor quality.[15]

New Formulations:
No new formulations were identified.

New FDA Safety Alerts:

Table 1. Description of New FDA Safety Alerts

Generic Name	Month / Year of Change	Labeling Addition or Change	Addition or Change and Mitigation Principles (if applicable)
All opioid formulations[16]	10/2019	Warnings/Precautions	Modifications to label to emphasize the risk for life-threatening respiratory depression in patients with sleep-related breathing disorders including sleep apnea and sleep-related hypoxemia. Additional warnings added for withdrawal symptoms associated with abrupt discontinuation. Gradual taper is recommended to minimize withdrawal syndrome.

References:

1. Toupin April K, Bisaillon J, Welch V, et al. Tramadol for osteoarthritis. *The Cochrane database of systematic reviews.* 2019;5:CD005522.
2. Yousef AA, Alzeftawy AE. The efficacy of oral piroxicam fast-dissolving tablets versus sublingual fentanyl in incident breakthrough pain due to bone metastases: a double-blinded randomized study. *Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer.* 2019;27(6):2171-2177.
3. HHS Guide for Clinicians on the Appropriate Dosage Reduction or Discontinuation of Long-Term Opioid Analgesics. U.S. Department of Health and Human Services. 2019. Available at https://www.hhs.gov/opioids/sites/default/files/2019-10/Dosage_Reduction_Discontinuation.pdf. Updated October 2019. Accessed January 4, 2020.
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6. Goplen CM, Verbeek W, Kang SH, et al. Preoperative opioid use is associated with worse patient outcomes after Total joint arthroplasty: a systematic review and meta-analysis. *BMC musculoskeletal disorders.* 2019;20(1):234.
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13. Abdel Shaheed C, Maher CG, McLachlan AJ. Efficacy and Safety of Low-dose Codeine-containing Combination Analgesics for Pain: Systematic Review and Meta-Analysis. *The Clinical journal of pain.* 2019;35(10):836-843.
14. Yang DZ, Sin B, Beckhusen J, Xia D, Khaimova R, Iliev I. Opioid-Induced Hyperalgesia in the Nonsurgical Setting: A Systematic Review. *American journal of therapeutics.* 2019;26(3):e397-e405.
15. Bennett MI, Eisenberg E, Ahmedzai SH, et al. Standards for the management of cancer-related pain across Europe-A position paper from the EFIC Task Force on Cancer Pain. *European journal of pain (London, England).* 2019;23(4):660-668.
16. Food and Drug Administration. Drug Safety-related Labeling Changes (SrLC). https://www.accessdata.fda.gov/scripts/cder/safetylabelingchanges/. Accessed January 3, 2020.

Appendix 1: Current Preferred Drug List

Long-Acting Opioids

Generic	Brand	Form	Route	PDL
fentanyl	DURAGESIC	PATCH TD72	TRANSDERM	Y
fentanyl	FENTANYL	PATCH TD72	TRANSDERM	Y
morphine sulfate	MORPHINE SULFATE ER	TABLET ER	ORAL	Y
morphine sulfate	MS CONTIN	TABLET ER	ORAL	Y
buprenorphine	BUPRENORPHINE	PATCH TDWK	TRANSDERM	N
buprenorphine	BUTRANS	PATCH TDWK	TRANSDERM	N
buprenorphine HCl	BELBUCA	FILM	BUCCAL	N
fentanyl	FENTANYL	PATCH TD72	TRANSDERM	N
hydrocodone bitartrate	ZOHYDRO ER	CAP ER 12H	ORAL	N
hydrocodone bitartrate	HYSINGLA ER	TAB ER 24H	ORAL	N
hydromorphone HCl	EXALGO	TAB ER 24H	ORAL	N
hydromorphone HCl	HYDROMORPHONE ER	TAB ER 24H	ORAL	N
levorphanol tartrate	LEVORPHANOL TARTRATE	TABLET	ORAL	N
methadone HCl	METHADONE HCL	ORAL CONC	ORAL	N
methadone HCl	METHADONE INTENSOL	ORAL CONC	ORAL	N
methadone HCl	METHADOSE	ORAL CONC	ORAL	N
methadone HCl	METHADONE HCL	SOLUTION	ORAL	N
methadone HCl	DOLOPHINE HCL	TABLET	ORAL	N
methadone HCl	METHADONE HCL	TABLET	ORAL	N
methadone HCl	METHADONE HCL	TABLET SOL	ORAL	N
methadone HCl	METHADOSE	TABLET SOL	ORAL	N
morphine sulfate	KADIAN	CAP ER PEL	ORAL	N
morphine sulfate	MORPHINE SULFATE ER	CAP ER PEL	ORAL	N
morphine sulfate	MORPHINE SULFATE ER	CPMP 24HR	ORAL	N
morphine sulfate	MORPHABOND ER	TAB ER 12H	ORAL	N
morphine sulfate/naltrexone	EMBEDA	CAP ER PO	ORAL	N
oxycodone HCl	OXYCODONE HCL ER	TAB ER 12H	ORAL	N
oxycodone HCl	OXYCONTIN	TAB ER 12H	ORAL	N
oxycodone myristate	XTAMPZA ER	CAP SPR 12	ORAL	N
oxymorphone HCl	OPANA ER	TAB ER 12H	ORAL	N
oxymorphone HCl	OXYMORPHONE HCL ER	TAB ER 12H	ORAL	N
tapentadol HCl	NUCYNTA ER	TAB ER 12H	ORAL	N
tramadol HCl	CONZIP	CPBP 17-83	ORAL	N
tramadol HCl	TRAMADOL HCL ER	CPBP 17-83	ORAL	N
tramadol HCl	CONZIP	CPBP 25-75	ORAL	N

tramadol HCl	TRAMADOL HCL ER	CPBP 25-75	ORAL	N
tramadol HCl	TRAMADOL HCL ER	TAB ER 24H	ORAL	N
tramadol HCl	TRAMADOL HCL ER	TBMP 24HR	ORAL	N

Short-Acting Opioids

Generic	Brand	Form	Route	PDL
acetaminophen with codeine	ACETAMINOPHEN W/CODEINE	ELIXIR	ORAL	Y
acetaminophen with codeine	CAPITAL W-CODEINE	ORAL SUSP	ORAL	Y
acetaminophen with codeine	ACETAMINOPHEN-CODEINE	SOLUTION	ORAL	Y
acetaminophen with codeine	ACETAMINOPHEN-CODEINE	TABLET	ORAL	Y
acetaminophen with codeine	TYLENOL-CODEINE NO.3	TABLET	ORAL	Y
acetaminophen with codeine	TYLENOL-CODEINE NO.4	TABLET	ORAL	Y
butorphanol tartrate	BUTORPHANOL TARTRATE	SPRAY	ORAL	Y
codeine sulfate	CODEINE SULFATE	TABLET	ORAL	Y
hydrocodone/acetaminophen	HYDROCODONE-ACETAMINOPHEN	SOLUTION	ORAL	Y
hydrocodone/acetaminophen	LORTAB	SOLUTION	ORAL	Y
hydrocodone/acetaminophen	HYDROCODONE/ACETAMINOPHEN	TABLET	ORAL	Y
hydrocodone/acetaminophen	LORCET	TABLET	ORAL	Y
hydrocodone/acetaminophen	LORCET HD	TABLET	ORAL	Y
hydrocodone/acetaminophen	LORCET PLUS	TABLET	ORAL	Y
hydrocodone/acetaminophen	NORCO	TABLET	ORAL	Y
hydromorphone HCl	HYDROMORPHONE HCL	SUPP.RECT	RECTAL	Y
hydromorphone HCl	DILAUDID	TABLET	ORAL	Y
hydromorphone HCl	HYDROMORPHONE HCL	TABLET	ORAL	Y
morphine sulfate	MORPHINE SULFATE	SOLUTION	ORAL	Y
morphine sulfate	MORPHINE SULFATE	SUPP.RECT	RECTAL	Y
morphine sulfate	MORPHINE SULFATE	TABLET	ORAL	Y
opium/belladonna alkaloids	BELLADONNA & OPIUM	SUPP.RECT	RECTAL	Y
opium/belladonna alkaloids	BELLADONNA-OPIUM	SUPP.RECT	RECTAL	Y
oxycodone HCl	OXYCODONE HCL	SOLUTION	ORAL	Y
oxycodone HCl	OXYCODONE HCL	TABLET	ORAL	Y
oxycodone HCl	ROXICODONE	TABLET	ORAL	Y
oxycodone HCl/acetaminophen	OXYCODONE W/ACETAMINOPHEN	CAPSULE	ORAL	Y
oxycodone HCl/acetaminophen	ENDOCET	TABLET	ORAL	Y
oxycodone HCl/acetaminophen	NALOCET	TABLET	ORAL	Y
oxycodone HCl/acetaminophen	OXYCODONE-ACETAMINOPHEN	TABLET	ORAL	Y
oxycodone HCl/acetaminophen	PERCOCET	TABLET	ORAL	Y
tramadol HCl	TRAMADOL HCL	TABLET	ORAL	Y

tramadol HCl	ULTRAM	TABLET	ORAL	Y
acetaminophen/caff/dihydrocod	ACETAMIN-CAFF-DIHYDROCODEINE	CAPSULE	ORAL	N
acetaminophen/caff/dihydrocod	ACETAMIN-CAFF-DIHYDROCODEINE	TABLET	ORAL	N
acetaminophen/caff/dihydrocod	DVORAH	TABLET	ORAL	N
acetaminophen/caff/dihydrocod	PANLOR	TABLET	ORAL	N
butalbit/acetamin/caff/codeine	BUTALB-ACETAMINOPH-CAFF-CODEIN	CAPSULE	ORAL	N
butalbit/acetamin/caff/codeine	BUTALB-CAFF-ACETAMINOPH-CODEIN	CAPSULE	ORAL	N
butalbit/acetamin/caff/codeine	FIORICET WITH CODEINE	CAPSULE	ORAL	N
codeine/butalbital/ASA/caffein	ASA-BUTALB-CAFFEINE-CODEINE	CAPSULE	ORAL	N
codeine/butalbital/ASA/caffein	ASCOMP WITH CODEINE	CAPSULE	ORAL	N
codeine/butalbital/ASA/caffein	BUTALBITAL COMPOUND-CODEINE	CAPSULE	ORAL	N
codeine/butalbital/ASA/caffein	FIORINAL WITH CODEINE #3	CAPSULE	ORAL	N
fentanyl	SUBSYS	SPRAY	SUBLINGUAL	N
fentanyl citrate	ACTIQ	LOZENGE HD	BUCCAL	N
fentanyl citrate	FENTANYL CITRATE	LOZENGE HD	BUCCAL	N
fentanyl citrate	LAZANDA	SPRAY/PUMP	NASAL	N
fentanyl citrate	ABSTRAL	TAB SUBL	SUBLINGUAL	N
fentanyl citrate	FENTORA	TABLET EFF	BUCCAL	N
hydrocodone/acetaminophen	HYDROCODONE W/ACETAMINOPHEN	ELIXIR	ORAL	N
hydrocodone/acetaminophen	ZAMICET	SOLUTION	ORAL	N
hydrocodone/acetaminophen	HYDROCODONE-ACETAMINOPHEN	TABLET	ORAL	N
hydrocodone/acetaminophen	VERDROCET	TABLET	ORAL	N
hydrocodone/acetaminophen	VICODIN	TABLET	ORAL	N
hydrocodone/acetaminophen	VICODIN ES	TABLET	ORAL	N
hydrocodone/acetaminophen	VICODIN HP	TABLET	ORAL	N
hydrocodone/ibuprofen	HYDROCODONE-IBUPROFEN	TABLET	ORAL	N
hydrocodone/ibuprofen	IBUDONE	TABLET	ORAL	N
hydrocodone/ibuprofen	REPREXAIN	TABLET	ORAL	N
hydrocodone/ibuprofen	XYLON 10	TABLET	ORAL	N
hydromorphone HCl	DILAUDID	LIQUID	ORAL	N
hydromorphone HCl	HYDROMORPHONE HCL	LIQUID	ORAL	N
ibuprofen/oxycodone HCl	OXYCODONE HCL-IBUPROFEN	TABLET	ORAL	N
meperidine HCl	MEPERIDINE HCL	SOLUTION	ORAL	N
meperidine HCl	DEMEROL	TABLET	ORAL	N
meperidine HCl	MEPERIDINE HCL	TABLET	ORAL	N
morphine sulfate	MORPHINE SULFATE	SYRINGE	ORAL	N
morphine sulfate	ARYMO ER	TAB PO ER	ORAL	N
oxycodone HCl	OXYCODONE HCL	CAPSULE	ORAL	N
oxycodone HCl	OXYCODONE HCL	ORAL CONC	ORAL	N
oxycodone HCl	OXYCODONE HCL	SYRINGE	ORAL	N

oxycodone HCl	OXAYDO	TABLET ORL	ORAL	N
oxycodone HCl	ROXYBOND	TABLET ORL	ORAL	N
oxycodone HCl/acetaminophen	OXYCODONE-ACETAMINOPHEN	TABLET	ORAL	N
oxycodone HCl/acetaminophen	PRIMLEV	TABLET	ORAL	N
oxycodone HCl/acetaminophen	ROXICET	TABLET	ORAL	N
oxycodone HCl/aspirin	OXYCODONE HCL-ASPIRIN	TABLET	ORAL	N
oxymorphone HCl	NUMORPHAN	SUPP.RECT	RECTAL	N
oxymorphone HCl	OPANA	TABLET	ORAL	N
oxymorphone HCl	OXYMORPHONE HCL	TABLET	ORAL	N
pentazocine HCl/naloxone HCl	PENTAZOCINE-NALOXONE HCL	TABLET	ORAL	N
propoxyphene nap/acetaminophen	PROPOXYPHENE NAPSYLATE W/APAP	TABLET	ORAL	N
tapentadol HCl	NUCYNTA	TABLET	ORAL	N
tramadol HCl/acetaminophen	TRAMADOL HCL-ACETAMINOPHEN	TABLET	ORAL	N
tramadol HCl/acetaminophen	ULTRACET	TABLET	ORAL	N
aspirin/codeine phosphate	ASPIRIN W/CODEINE	TABLET	ORAL	

Appendix 2: New Comparative Clinical Trials

A total of 204 citations were manually reviewed from the initial literature search. After further review, all except one trial was excluded because of wrong study design (e.g., observational), comparator (e.g., no control or placebo-controlled), or outcome studied (e.g., non-clinical). This trial is summarized in the table below and the full abstract is included in **Appendix 3**.

Table 1. Description of Randomized Comparative Clinical Trials.

Study	Comparison	Population	Primary Outcome(s)	Results
Yousef, et al.[2] DB, AC, RCT N=100 Duration: 30 days	1. Fentanyl 200 µg sublingual tablet 2. Piroxicam 20 mg fast-dissolving tablets Dose was titrated over 2 weeks to achieve a 50% reduction in pain episodes. Average dose after titration was not reported.	Patients with breakthrough cancer pain related to bone metastases on stable long-term analgesia Location: Egypt	Reduction in pain intensity using the VAS (range 0-10) Frequency of breakthrough pain attacks per day Onset of pain relief	Mean VAS at 1 month 1. 3.37 (SD 0.74) 2. 3.47 (SD 0.76) P=0.510 Breakthrough pain attacks at 1 month 1. 21.74 (SD 5.34) 2. 22.16 (SD 4.97) P=0.685 Mean onset of pain relief 1. 6.10 (SD 1.23) 2. 17.14 (SD 3.76) P<0.001

Abbreviations: AC = active comparator; DB = double blind; RCT = randomized clinical trial; VAS = visual analog scale

Appendix 3: Abstracts of Comparative Clinical Trials

Yousef AA, Alzeftawy AE. The efficacy of oral piroxicam fast-dissolving tablets versus sublingual fentanyl in incident breakthrough pain due to bone metastases: a double-blinded randomized study. *Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer.* 2019;27(6):2171-2177.

PURPOSE: Breakthrough pain (BTP) is a transient exacerbation of pain occurring in a patient with chronic, persistent pain. The most common type is incident pain that is mostly related to bone metastases. The oral mucosa is an attractive route for drug delivery. Sublingual fentanyl preparations are a very attractive agent in controlling attacks of BTP due to its rapid absorption through the oral mucosa. Non-steroidal anti-inflammatory drugs (NSAIDs) play a key role as a first step in treatment of cancer pain; piroxicam sublingual formulations could be a useful alternative in controlling incident pain. Our study hypothesis is to evaluate the efficacy of sublingual fentanyl versus oral piroxicam fast-dissolving tablets in patients with incident pain and its impact on functional status.
PATIENTS AND METHODS: A cohort of 100 adults of both genders suffering from bone metastases. Patients were assigned to receive either sublingual fentanyl tablet (group 1) or oral piroxicam fast-dissolving tablets (group 2). The pain intensity reduction on a 0-10 visual analog scale (VAS), frequency of BTP attacks, and onset of pain relief. Secondary end points included the functional interference items of the Brief Pain Inventory (BPI).
RESULTS: There is no significant difference between the two groups regarding the patients' demographics. Significant decline of the VAS in each group in comparison to the pretreatment values (p = 0.001). Non-significant changes of the VAS, duration of pain attacks, and number of rescue doses in comparing both groups were measured. There was significant reduction in group 2 BPI regarding the relation with others, sleep pattern and enjoyment of life parameters at 2 and 4 weeks (p = 0.001).
CONCLUSION: Our study demonstrated that oral piroxicam fast-dissolving tablet is an analgesic alternative to sublingual fentanyl in patients with bone metastasis to control incidental BTP attacks with more favorable cost-benefit values.

Appendix 4: Medline Search Strategy

Ovid MEDLINE(R) ALL 1946 to January 02, 2020

1	exp Analgesics, Opioid/ae, po, tu, to [Adverse Effects, Poisoning, Therapeutic Use, Toxicity]	45855
2	limit 1 to yr="2019 -Current"	977
3	limit 2 to (english language and humans)	884
4	limit 3 to (clinical study or clinical trial, all or clinical trial, phase iii or clinical trial, phase iv or clinical trial or comparative study or controlled clinical trial or guideline or meta analysis or multicenter study or practice guideline or randomized controlled trial or "systematic review")	204

Appendix 5: Key Inclusion Criteria

Population	Patients needing analgesia management
Intervention	short-acting or long-acting oral opioids
Comparator	Other opioids or analgesics
Outcomes	Improved pain control, symptoms, function, quality of life, or adverse events
Timing	Follow-up of at least 30 days
Setting	Outpatient

Long-acting Opioid Analgesics

Goals:

- Restrict use of long-acting opioid analgesics to OHP-funded conditions with documented sustained improvement in pain and function and with routine monitoring for opioid misuse and abuse.
- Restrict use of long-acting opioid analgesics for conditions of the back and/or spine due to evidence of increased risk vs. benefit.
- 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 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:

- 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
AVINZA	1 dose/day
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	2 doses/day
KADIAN	2 doses/day
MORPHABOND	2 doses/day
MS CONTIN	3 doses/day
NUCYNTA ER	2 doses/day
OPANA ER	2 doses/day
OXYCONTIN	2 doses/day

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

Approval Criteria		
1. What is the patient's diagnosis?	Record ICD10 code	
2. Is the request for a patient already established on any opioid treatment for >6 weeks (long-term, chronic treatment)?	**Yes**: Go to **Renewal Criteria**	**No**: Go to #3

3. Is the diagnosis funded by the OHP? Note: Management of pain associated with *back or spine conditions with long-acting opioids* is not funded by the OHP*. Other conditions, such as fibromyalgia, TMJ, neuropathy, tension headache and pelvic pain syndrome are also not funded by the OHP.	**Yes:** Go to #4	**No:** Pass to RPh. Deny; not funded by the OHP. Note: Management of opioid dependence is funded by the OHP.
4. Is the requested medication a preferred agent?	**Yes:** Go to #6	**No:** Go to #5
5. Will the prescriber change to a 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:** Inform prescriber of covered alternatives in class.	**No:** Go to #6
6. 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 #7
7. Is the prescription for pain associated with 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 #8

8. Does the total daily opioid dose exceed 90 MME (see Table 1)?	**Yes:** Pass to RPh. Deny; medical appropriateness. Note: Management of opioid dependence is funded by the OHP.	**No:** Go to #9
9. 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 month that opioid prescribing is appropriate?	**Yes:** Go to #10	**No:** Pass to RPh. Deny; medical appropriateness
10. Is the patient concurrently on other short- or long-acting opioids (patients may receive a maximum of one opioid product regardless of formulation)? Note: There is insufficient evidence for use of concurrent opioid products (e.g., long-acting opioid with short-acting opioid).	**Yes:** Pass to RPh. Deny; medical appropriateness Note: Management of opioid dependence is funded by the OHP.	**No:** Go to #11
11. 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 #12
12. Does the prescription exceed quantity limits applied in Table 2 (if applicable)?	**Yes:** Pass to RPh. Deny; medical appropriateness	**No:** Go to #13

13. 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 #14 Document tool used and score vs. baseline: _____	**No:** Pass to RPh. Deny; medical appropriateness. Note: Management of opioid dependence is funded by the OHP.
14. Has the patient had a urinary drug screen (UDS) within the past 3 months to verify absence of illicit drugs and non-prescribed opioids?	**Yes:** Approve for up to 90 days.	**No:** Pass to RPh. Deny; medical appropriateness. Note: Management of opioid dependence is funded by the OHP.

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. Is there documentation indicating it is **unsafe** to initiate a taper at this time?	**Yes:** Go to #5 Document provider attestation and rationale	**No:** Pass to RPh. Deny; medical appropriateness

5. 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 #6	**No:** Pass to RPh. Deny. Medical appropriateness
6. 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 #7	**No:** Pass to RPh. Deny. Medical appropriateness
7. 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 #9 Document tool used and score vs. baseline: _____	**No:** Go to #8
8. Has the patient been referred for alternative non-pharmacologic modalities of pain treatment (e.g., physical therapy, supervised exercise, spinal manipulation, yoga, or acupuncture)?	**Yes:** Go to #9	**No:** Pass to RPh. Deny. Medical appropriateness
9. Is the request for an increased cumulative dose compared to previously approved therapy or average dose in the past 6 weeks?	**Yes:** Go to #10	**No:** Go to #13
10. Does the prescription exceed quantity limits applied in Table 2 (if applicable)?	**Yes:** Pass to RPh. Deny; medical appropriateness	**No:** Go to #11
11. Does the total cumulative daily opioid dose exceed 90 MME (see Table 1)?	**Yes:** Pass to RPh. Deny; medical appropriateness	**No:** Go to #12

12. Is there documented rationale (e.g., new acute injury) to support the increase in dose?	**Yes:** Go to #13	**No:** Pass to RPh; deny; medical appropriateness
13. 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 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	**Yes:** Go to #14 Document number of risk factors	**No:** Go to #15
14. Has the member been prescribed or have access to naloxone?	**Yes:** Go to #15	**No:** Pass to RPh. Deny. Medical appropriateness
15. Does the patient have a pain contract on file with the prescriber?	**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 0: 6 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: *2/20 (SS), 9/19 (DM), 3/17 (MH); 11/16; 05/16*
Implementation: *3/1/2020; 10/1/19*

Short-acting Opioid Analgesics

Goals:
- Restrict use of short-acting opioid analgesics for acute conditions funded by the OHP.
- 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 #3	**No:** Pass to RPh. Deny; not funded by the OHP. Note: Management of opioid dependence is funded by the OHP.
4. Is the requested medication a preferred agent?	**Yes:** Go to #6	**No:** Go to #5
5. Will the prescriber change to a 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:** Inform prescriber of covered alternatives in class.	**No:** Go to #6
6. 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 #7
7. 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 #8

8. 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 #9
9. 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 #10
10. 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 month and verified that opioid prescribing is appropriate?	**Yes:** Go to #11	**No:** Pass to RPh. Deny; medical appropriateness.
11. 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 #12

12. 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 #13	**No:** Pass to RPh. Deny; medical appropriateness
13. Is the opioid prescription for pain associated with a back or spine condition?	**Yes:** Go to #14	**No:** Approve for up to 30 days
14. 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 spinal manipulation, physical therapy, yoga, weight loss, massage therapy, or acupuncture?	**Yes:** Go to #15	**No:** Pass to RPh. Deny; medical appropriateness
15. Is this the first opioid prescription the patient has received for this pain condition?	**Yes:** Approve for up to 7 days not to exceed 90 MME	**No:** Go to #16
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:** Approve for up to 7 days not to exceed 90 MME	**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. Is there documentation indicating it is **unsafe** to initiate a taper at this time?	**Yes:** Go to #5 Document provider attestation and rationale	**No:** Pass to RPh. Deny; medical appropriateness
5. 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 #6	**No:** Pass to RPh. Deny. Medical appropriateness
6. 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 #7	**No:** Pass to RPh. Deny. Medical appropriateness
7. 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 #9 Document tool used and score vs. baseline: _____	**No:** Go to #8
8. Has the patient been referred for alternative non-pharmacologic modalities of pain treatment (e.g., physical therapy, supervised exercise, spinal manipulation, yoga, or acupuncture)?	**Yes:** Go to #9	**No:** Pass to RPh. Deny. Medical appropriateness

9. 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 #10	**No:** Go to #12
10. Does the total cumulative daily opioid dose exceed 90 MME (see Table 1)?	**Yes:** Pass to RPh. Deny; medical appropriateness	**No:** Go to #11
11. Is there documented rationale (e.g., new acute injury) to support the increase in dose?	**Yes:** Go to #12	**No:** Pass to RPh; deny; medical appropriateness
12. 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 or prescribed concurrent short- and long-acting opioids c. Recent urine drug screen indicating illicit or non-prescribed opioids	**Yes:** Go to #13 Document number of risk factors	**No:** Go to #14
13. Has the member been prescribed or have access to naloxone?	**Yes:** Go to #14	**No:** Pass to RPh. Deny. Medical appropriateness

14. Does the patient have a pain contract on file with the prescriber?	**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 0: 6 months	**No:** Pass to RPh. Deny; medical appropriateness

*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: *2/20 (SS), 9/19 (DM), 11/16 (AG)*
Implementation: *3/1/2020; 10/1/2019; 8/21/17*