Drug Use Research & Management Program
Oregon State University, 500 Summer Street NE, E35
Salem, Oregon 97301-1079
Phone 503-947-5220 | **Fax** 503-947-1119

Drug Use Evaluation: Methadone

Research Questions:

- What are the characteristics of patients with fee-for-service (FFS) methadone claims before and after the removal of methadone from the Oregon Medicaid FFS preferred drug list (PDL)?
- How has utilization of methadone changed after its removal from the PDL?
- What is the incidence of hospitalization and ED visits due to methadone overdose before and after the removal of methadone from the PDL?
- What is the incidence of hospitalization and ED visits due to heroin overdose before and after removal of methadone from the PDL?

Conclusions:

- Utilization of methadone for pain management has decreased substantially since the removal of methadone from the PDL.
- Since the change in methadone PDL status, there has been a trend in decreased hospitalizations for methadone overdose and increased hospitalizations for heroin overdose.

Recommendations:

- Maintain status of methadone as a non-preferred agent on the Oregon Medicaid FFS PDL.

Background:

Opioid misuse in the United States (U.S.) has increased over the past two decades.[1] In 2012, Oregon had the highest rate of non-medical use of prescription pain medications in the U.S. [1] Data from the Oregon Prescription Drug Monitoring Program (PDMP) show that almost 25% of Oregonians received a prescription for opioid medications in 2012.[1] Increased opioid prescribing has led to a higher incidence of overdose. Between 2000 and 2012, about 322 people per year in Oregon died due to unintentional and undetermined drug overdose. [1] Methadone was associated with over 50% of prescription opioid-related deaths from 2000-2011 in Oregon.[1]

Methadone is indicated for chronic pain as well as for opioid use disorder through opioid treatment programs. It carries a FDA Black Box warning for increased risk of death and risk of abuse and misuse.[2] Its long duration of action and affordability may be reasons for its use for pain management. However, because of methadone's long half-life, variable pharmacokinetics, and delayed onset, it can can lead to accumulation with dose titration, resulting in respiratory depression or cardiac arrest.[3] Retail distribution of methadone more than doubled between 2000 and 2006; methadone-associated overdose deaths showed a similar increase.[1] In December 2006, the Food and Drug Administration (FDA) issued a Public Health Advisory to encourage reporting of death and life-threatening adverse events in patients receiving methadone. In 2012, the Centers for Disease Control and Prevention (CDC) recommended that insurance formularies should not list methadone as a preferred drug for the treatment for chronic non-cancer pain and be reserved for use in selected circumstances only (such as cancer pain or palliative care).[4] A retrospective analysis found that those receiving methadone for non-cancer pain relief had 46% increased risk of overdose dose compared to those receiving alternative therapy.[5] Therefore, the recommendation to remove methadone from the Oregon Medicaid FFS PDL was made in July 2013.

Author: Tiffany Tsai, PharmD Date: May 2018

The CDC recently assessed state Medicaid PDL policies and their effect on methadone prescribing and methadone-related deaths.[6] Overall, there was a large decline in methadone-related overdose deaths between 2007 and 2014. However, rates of fatal and nonfatal methadone overdose in South Carolina, which did not include methadone on the PDL, was significantly lower than in North Carolina ($p<0.001$) and Florida ($p<0.001$), which still included methadone on the PDL. Rates of fatal and nonfatal methadone overdose were similar between North Carolina and Florida.[6] This analysis suggests that addition of methadone to the PDL is associated with increased rates of methadone overdose in Medicaid recipients.

While prescription opioid abuse remains a problem in the U.S., heroin use has also increased in the past decade. Heroin is readily available and is more affordable than prescription opioids, making it an attractive alternative in opioid dependent persons.[7] The Healthcare Cost and Utilization Project found that while emergency department (ED) and inpatient discharge rates for prescription opioid overdoses began to decline around 2010, discharge rates for heroin overdoses sharply increased around 2008.[8] One factor that contributes to heroin use is availability and affordability.[7] Heroin users often transition from prescription opioid use.[7] A study of intravenous (IV) drug users found a significant rate of users reported problematic prescription opioid use before starting heroin, including 47% of IV drug users in Portland, Oregon.[9] Furthermore, between 2008 and 2010, 82.6% of heroin users report using prescription opioids prior to heroin compared to 64.1% between 2002 and 2004.[10] With increased restriction on availability of oral prescription opioids such as methadone, use of heroin may continue to increase and result in increased hospitalizations for heroin overdose.

The goal of this report is to evaluate the impact of removal of methadone from Oregon Medicaid's PDL on methadone utilization and assess rate of overdoses resulting in hospital admissions or ED visits due to methadone or heroin.

Methods:

This is a retrospective pre/post cohort study to evaluate the impact of making methadone non-preferred. Utilization of methadone over time was evaluated by including FFS pharmacy claims from January 2011 through June 2017 and reported as claims per enrolled member per month x1000.

Patient demographics were reported on all patients with a paid FFS drug claim for methadone from January 1, 2013 to December 31, 2013 (pre policy group) and from January 1, 2014 to December 31, 2014 (post policy group). A year before and after the policy change was chosen since it is difficult to draw conclusions about an effect after a year. Patients were excluded if they had any of the following benefit packages which indicate Medicare part D coverage (benefit packages BMM, BMD, MND, CWM, SMF, SNB or MED). Patients were also excluded if they had a diagnosis of palliative care with a terminal diagnosis or with cancer-related pain at any time from a year prior to their first pharmacy claim to the end of their respective period (**ICD 10**: C690-C799; C800-C802 and **ICD 9**: V66.7, 799.3, 140-239, 338.3). Number of patients receiving more than 90 morphine milligram equivalent doses of methadone was also captured.

To capture the incidence of hospitalizations or ED visits due to methadone and heroin overdose, a separate cohort to analyze this research question was compiled. All Medicaid patients admitted to a hospital or presenting to an ED with an ICD code for methadone poisoning or heroin poisoning (**Table 1**) from January 2011 through June 2017 were included and depicted as a rate per enrolled member per month x10,000.

Table 1: ICD Codes for Methadone and Heroin Poisoning

Description	ICD-9 code	ICD-10 code
Poisoning by methadone	965.02, E850.1	T40.3X1A-4A
Poisoning by heroin	965.01	T40.1X1A-4A

Results:

Patient demographics are similar among patients receiving methadone for pain management before and after the change in methadone PDL status (**Table 2**). There was a 58% reduction of patients who had claims for methadone after the status change (197 patients in 2013 and 83 patients in 2014). The majority of patients both pre- and post-policy change were between the ages of 18 to 54 years, and over 65% were white. Similarly, in both cohorts, about half the patients received more than 90 morphine milligram equivalents per day.

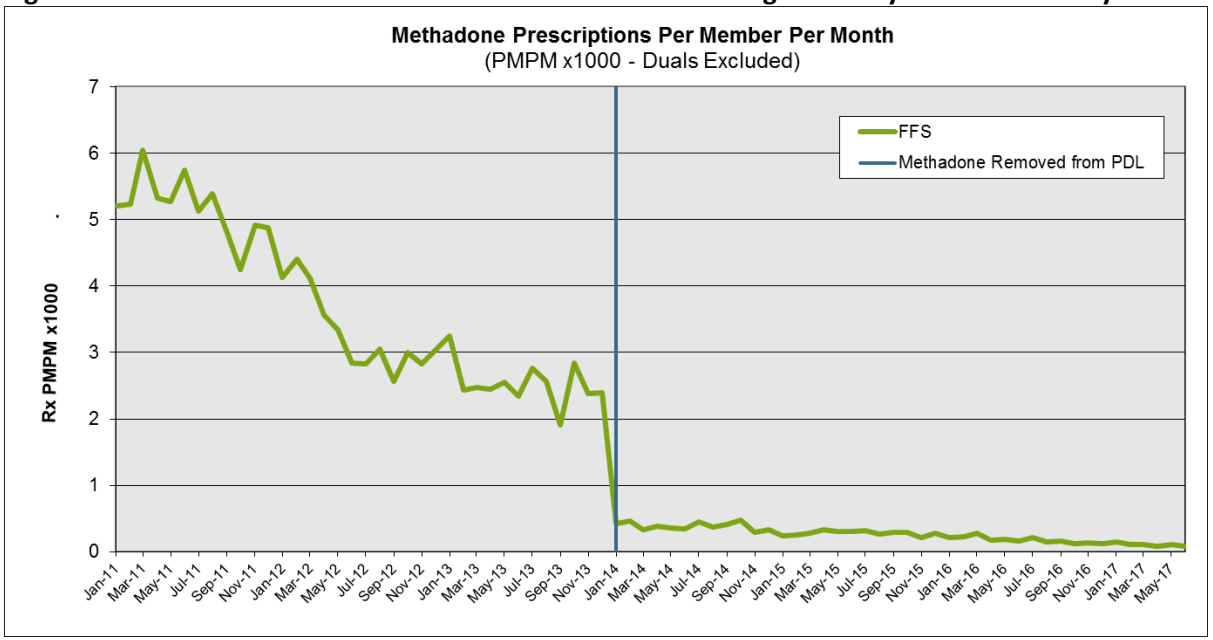
Table 2. Demographics of Patients with FFS Methadone Claims

Demographics	Pre Policy 2013 (n=197)	Post Policy 2014 (n=83)
Average age	45	47
Age (years)	n (%)	n (%)
0-17	5 (2.5)	1 (1.2)
18-54	139 (70.6)	57 (68.7)
55-64	50 (25.4)	24 (28.9)
65+	3 (1.5)	1 (1.2)
Female	121 (61.4)	44 (53)
White	131 (66.5)	57 (68.7)
Methadone dose >90 MME/day	94 (47.7)	47 (56.6)

Abbreviations: MME = morphine milligram equivalent

Figure 1 displays overall utilization (as methadone prescriptions per member per month x1000) over time from 2011 to 2017. Utilization sharply decreased around the time of the change in methadone PDL status, with 125 claims in December 2013 out of 52,106 members (2.4 PMPM x1000) to 48 claims in January 2014 out of 112,554 members (0.43 PMPM x1000). The number of claims was reduced after the change in methadone status even though the number of members increased by over 116% due to the Affordable Care Act (ACA) Medicaid expansion at that time. After 2014, utilization remained low with a downward trend.

Figure 1. FFS Methadone Utilization Before and After the Change in Policy Effective January 2014



Despite the decline in overall utilization, the absolute number of patients with hospitalizations for methadone or heroin overdose increased from 2013 to 2014 in both FFS and CCO patients as depicted in **Table 3.** However, the PMPM of methadone poisoning decreased in FFS patients from 2013 to 2014.

Table 3. Number of Patients with Hospitalizations or ED Visits for Methadone or Heroin Poisoning

Patient Hospitalizations/ED Visits	**Pre Policy 2013**		**Post Policy 2014**	
	n	PMPMx10,000	n	PMPMx10,000
Methadone Poisoning	n=86	1.38	n=134	1.41
FFS	19	2.45	29	2.09
CCO	67	1.23	107	1.32
Heroin Poisoning	n=145	2.33	n=432	4.54
FFS	27	3.48	102	7.36
CCO	118	2.16	337	4.14

Although there appears to be extensive variability in rates of hospitalization for both methadone and heroin poisoning (**Figures 2 and 3)**, the linear trend reveals an overall downward trend in hospitalizations/ED visits from methadone overdose and an upward trend in hospitalizations/ED visits from heroin overdose. For methadone poisoning, the decreasing trend was similar before and after methadone was removed from the PDL (**Figure 2**). However, for heroin poisoning, the rate of increase was higher after methadone was removed from the PDL (**Figure 3**).

Author: Tiffany Tsai, PharmD

Date: May 2018

Figure 2. Patients Hospitalized for Methadone Poisoning from 2011 to 2017 (Per-Member Per-Month x10,000)

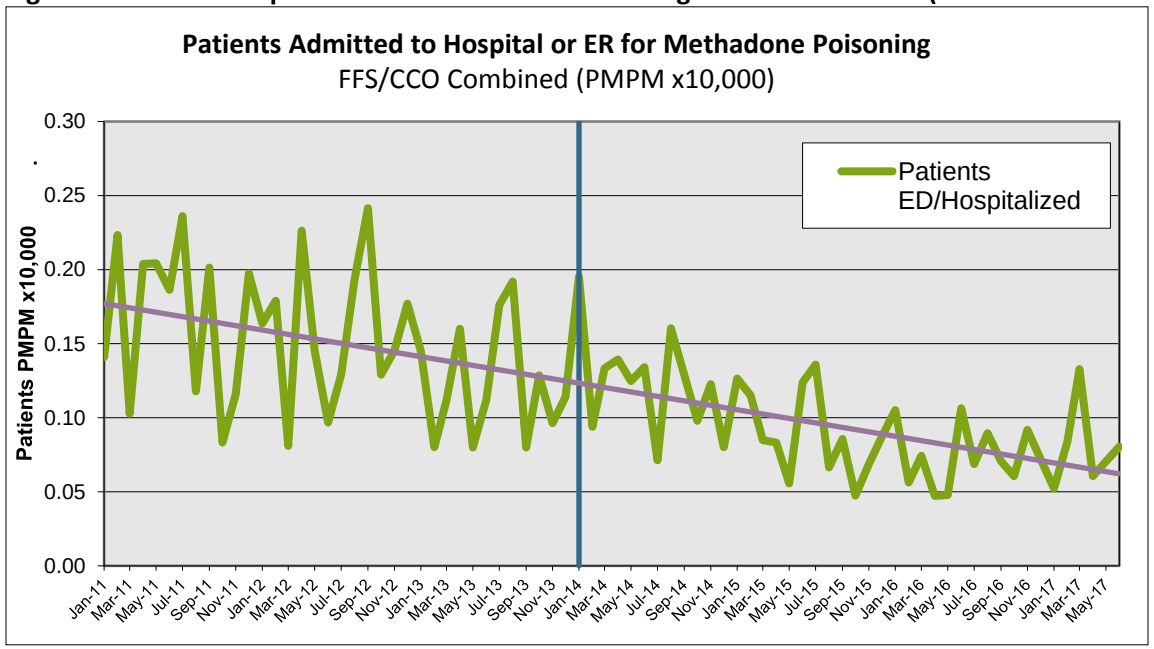
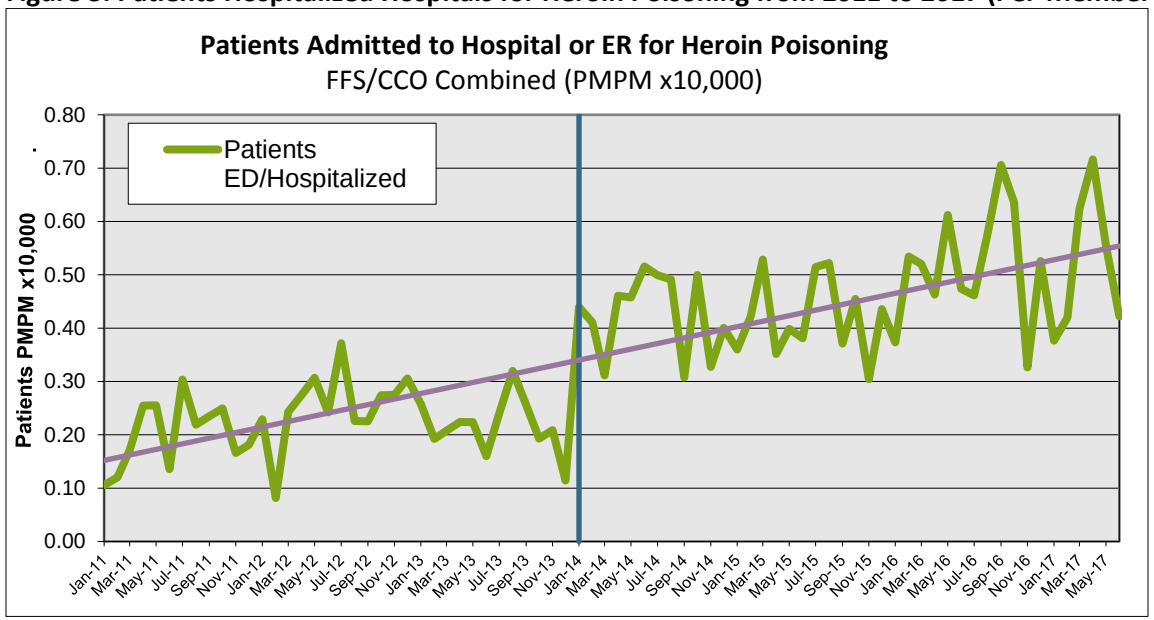


Figure 3. Patients Hospitalized Hospitals for Heroin Poisoning from 2011 to 2017 (Per-Member Per-Month x10,000)



Author: Tiffany Tsai, PharmD

Date: May 2018

Discussion

Patient demographics are similar among patients receiving methadone before and after the change in PDL status. Utilization of methadone sharply decreased at the start of 2014 when methadone was removed from the PDL. However, there did not seem to be a change in the number of patients receiving high dose methadone (≥ 90 morphine milligram equivalent [MME]). The CDC guidelines recommend avoiding daily doses ≥ 90 MME which significantly increase risk for motor vehicle accidents, opioid use disorder, and overdose.[4] There was already evidence of decrease in methadone utilization between 2011 and 2012, even before the change in PDL status. This may be due to CDC and FDA efforts in provider education leading up to the change in methadone PDL status. The ACA was enacted in 2014, which resulted in more Medicaid enrollees in Oregon around the time of this PDL change. The absolute number of methadone claims decreased in 2014 despite the significant increase in patients enrolled in Medicaid FFS, resulting in a significantly reduced proportion of patients with methadone claims.

Despite the decreased utilization, there did not appear to be a significant difference in the absolute number of hospitalizations due to methadone poisoning or heroin poisoning in 2013 and 2014. The impact of the change in PDL status of methadone on both methadone and heroin poisonings may not be evident because of the change in number of Medicaid enrollees due to the ACA. However, as shown in Figure 2 and 3, the amount of patients (per member per month x10,000) admitted for methadone poisonings has trended downward from 2011 to 2017 while the patients admitted for heroin poisonings has trended upwards. The rate of decrease in ED visits or hospitalizations from methadone poisoning was similar before and after the change in methadone's PDL status. However, the rate of increase in ED visits or hospitalizations for heroin poisoning was higher after methadone was removed from the PDL.

This increasing trend in heroin overdose may be influenced by reduced access to prescription opioids. While payers may restrict availability of methadone and other prescription opioids, they are unable to restrict the use of heroin as a substitute. However, no firm conclusions can be made as to whether the increased heroin hospitalizations are due to the removal of methadone from the PDL or due to other factors such as heroin cost or availability.

Limitations:

This evaluation is subject to the limitations of all claims-based retrospective analyses. This evaluation does not show if the hospitalizations were from repeat admissions of the same patient. It also does not capture overdoses that are reversed in the community. The percentage of overdoses captured is likely only a small proportion of all overdoses, and we are unable to capture deaths due to heroin or methadone overdose due to limitations in the data. Furthermore, this analysis did not capture any methadone prescriptions purchased with cash. It is possible that patients were paying out-of-pocket for their methadone prescription after the change in PDL status. Additionally, the ACA Medicaid expansion could result in differences between the two cohorts of patients compared in this analysis.

References:

1. 2014 Drug Overdose Deaths, Hospitalizations, Abuse or Dependency among Oregonians http://www.oregon.gov/oha/ph/DiseasesConditions/InjuryFatalityData/Documents/oregon-drug-overdose-report.pdf
2. Food and Drug Administration, "Methadone Hydrochloride Approved Label 4/14/2014," accessed April 2, 2018, http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/090707Orig1s003lbl.pdf.
3. Ray WA, Chung CP, Murray KT, Cooper WO, Hall K, Stein CM. Out-of-hospital mortality among patients receiving methadone for noncancer pain. JAMA Intern Med. 2015;175(3):420-7.
4. Centers for Disease Control and Prevention, "Vital Signs: Risk for Overdose from Methadone Used for Pain Relief – United States, 1999–2010," Morbidity and Mortality Weekly Report 61, no. 26 (2012): 493-497, http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6126a5.htm.
5. Ray W, et al., "Out-of-Hospital Mortality among Patients Receiving Methadone for Noncancer Pain." *JAMA Intern Med*. 2015;175(3):420-7

Author: Tiffany Tsai, PharmD Date: May 2018

6. Faul M, Bohm M, Alexander C. Methadone Prescribing and Overdose and the Association with Medicaid Preferred Drug List Policies — United States, 2007–2014. MMWR Morb Mortal Wkly Rep 2017;66:320–323. DOI: http://dx.doi.org/10.15585/mmwr.mm6612a2
7. Kanouse AB, Compton P. The epidemic of prescription opioid abuse, the subsequent rising prevalence of heroin use, and the federal response. J Pain Palliat Care Pharmacother. 2015;29(2):102-14.
8. Tedesco D, Asch SM, Curtin C, et al. Opioid Abuse and Poisoning: Trends in Inpatient and Emergency Department Discharges. Health Aff (Millwood). 2017;36(10):1748-1753.
9. Pollini RA, Banta-Green CJ, Cuevas-Mota J, Metzner M, Teshale E, Farfein RS. Problematic use of prescription-type opioids prior to heroin use among young heroin injectors. Subst Abuse Rehabil. 2011;2:173–180.
10. Jones CM. Heroin use and heroin use risk behaviors among nonmedical users of prescription opioid pain relievers—United States, 2002–2004 and 2008–2010. Drug Alcohol Depend. 2013;132:95–100.

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:

90 days (except 12 months for end-of-life or cancer-related pain)

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 (ICD10 C6900-C799; C800-C802) are exempt from this PA.
- This PA does not apply to pediatric use of codeine products, which is subject to separate clinical PA criteria.

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

Opioid	90 MME/day	Notes
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.)
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.
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 Quantity 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
NUCYNTA ER	2 doses/day
OPANA ER	2 doses/day
OXYCONTIN	2 doses/day
TROXYCA ER	2 doses/day

Drug Product	Quantity Limit
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 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, tension headache and pelvic pain syndrome are also 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.

3. Is the requested medication a preferred agent?	**Yes:** Go to #5	**No:** Go to #4
4. 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 #5
5. Is the patient being treated for cancer-related pain (ICD10 G89.3) or under palliative care services (ICD10 Z51.5) with a life-threatening illness or severe advanced illness expected to progress toward dying?	**Yes:** Approve for up to 12 months	**No:** Go to #6
6. 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 3 months that the patient has been prescribed opioid analgesics by only a single prescribing practice or prescriber?	**Yes:** Go to #7	**No:** Pass to RPh. Deny; medical appropriateness
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 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 #10
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. 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 #12 Document tool used and score vs. baseline: _____	**No:** Pass to RPh. Deny; medical appropriateness. Note: Management of opioid dependence is funded by the OHP.
12. Has the patient had a urinary drug screen (UDS) within the past 1 year 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.

*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 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.

Author: Tiffany Tsai, PharmD

Date: May 2018

Selecting the optimal timing and approach to tapering depends on multiple factors. The rate of opioid taper should be based primarily on safety considerations, and special attention is needed for patients on high dose opioids, 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 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 the rate of taper based on safety considerations:
    a. Immediate discontinuation 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. Start with a taper of ≤10% of the original dose per week 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 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.
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: *3/17 (MH); 11/16; 05/16*

Implementation: *Phase implementation initiated 8/21/17*