



UNIVERSITY OF UTAH
COLLEGE OF PHARMACY
L. S. SKAGGS PHARMACY INSTITUTE

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LONG-ACTING OPIOIDS FOR CHRONIC NON-CANCER PAIN

Opiate agonists

Fentanyl transdermal patches

Hydrocodone ER

Hydromorphone ER

Methadone

Morphine Sulfate ER

Oxycodone ER

Oxymorphone ER

Tapentadol ER

Tramadol ER

Drug Regimen Review Center

Joanita Lake B.Pharm, MSc EBHC (Oxon), Clinical Pharmacist

Joanne LaFleur, PharmD, MSPH, Associate Professor

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Introduction

As comprehensively described in the short-acting opioids for non-cancer pain report, prescription opioid misuse and abuse and the associated consequences (including overdoses) is a big problem that needs to be addressed.¹⁻⁹ It is important to recall that it is not only patients that are at risk of overdose, but also others when opioids are diverted.¹⁰

The Utah Medicaid DUR Board agreed on quantity limitations for short-acting (SA) opioids to allow sufficient quantities to ensure patients have access to appropriate pain medications whilst limiting access to excessive quantities that could lead to overdose or diversion. This review will discuss the available evidence for dosages and quantity limitations similar to the short-acting opioid report of last month, but will focus on the long-acting opioids (opiate agonists).

In general, the current standard of practice for prescribing opioids for chronic pain is the use of a long-acting opioid for around-the-clock pain management, and if necessary, a short-acting opioid for break-through pain. The reasoning or advantages of using long-acting (LA) opioids have been that they “(a) provide more consistent and stable serum levels, and therefore more stable analgesia, (b) enhance compliance secondary to reduced frequency of dosing, (c) are less likely to be ‘abused’ as they are not as often associated with euphoria, and (d) less likely to activate an ‘addiction’ process or pattern of abuse.”¹¹

The following sections in the short-acting opioids for chronic non-cancer pain provide useful background information and will not be repeated in this report:

- Opioid classes and mechanism of action
- Definitions relating to opioid misuse and abuse
- Opioid therapy for chronic non-cancer pain including pathophysiology and etiology of pain (e.g. nociceptive or neuropathic)
- Table 2. Agents preferable to opioids in chronic non-malignant pain
- Opioid prescribing and use
- Factors to consider regarding appropriate opioid use (opioid tolerance; opioid sharing, storage and disposing of opioid medications, repeated dose escalations)

Information and evidence that was described and discussed in the previous report included the following:

- “Opioid therapy for chronic noncancer pain (CNCP) is controversial due to concerns regarding long-term effectiveness and safety, particularly the risk of tolerance, dependence, or abuse.”¹²
- In theory, opioids have no maximum ceiling dose and the short-acting opioids report includes what the various guidelines and sources state about “dangerous” dosage levels. Various factors affect decisions regarding appropriate doses and type of opioid used. Variability and limitations of conversion factors/ratios were also discussed in the previous report.
- The CDC guidelines advise caution when increasing dosage to ≥ 50 morphine milligram equivalents (MME), and recommend to avoid dosages ≥ 90 MME.¹³ Some guidelines like the American Pain Society/American Academy of Pain Medicine and the Canadian guidelines consider higher doses (200 mg/day MME) a “high” dose or a “watchful” dose.^{14,15} The CDC guidance also states that only the quantity needed for the expected duration of pain severe enough to require opioids should be prescribed. “Three days or less will often be sufficient; more than 7 days will rarely be needed.”
- There is not much evidence specifically regarding dosage in Cochrane/PubMed. No Cochrane reviews or other reviews meeting the criteria for the Database of Abstracts of Reviews of Effects (DARE) were identified regarding dosage/quantity limitations (maximum daily dosage) or the association of prescribed opioid dosages and optimal treatment or adverse outcomes in chronic non-cancer pain.

Cochrane Systematic reviews identified regarding opioid use in chronic non-cancer pain include chronic low back pain, neuropathic pain, phantom limb pain, rheumatoid and osteoarthritis pain.

- It should be recognized that opioid overdoses are associated with higher opioid doses (increases with increasing doses), higher prescription painkiller sales per person, multiple prescribers, and more nonmedical use of prescription painkillers.^{1,16-18}
- Some of the challenges have been discussed as well such as patients already receiving high-dose opioids, patients already receiving both benzodiazepines and opioids, excessive prescribing, and issues relating to misuse/abuse/diversions including multiple prescribers.
- The CDC guidelines which have been endorsed by the FDA re-iterate “well-accepted medical principles of drug prescribing: to use the lowest effective dose for the shortest possible duration.”¹⁰ Opioid use is associated with serious risks (including misuse, abuse and overdose), and excessive prescriptions and fills lead to leftover medications which is an important source of opioids that are misused or diverted.^{19,20}
- Some safety information that apply to both LA and SA opioids

Methodology

The Agency for Healthcare Research and Quality (AHRQ; www.guideline.gov), Cochrane Library, the FDA website (including product labeling information), PubMed, UpToDate, Micromedex, Lexicomp, the Institute for Clinical and Economic Review (ICER) website, the National Institute for Health and Clinical Excellence (NICE) website, and ClinicalKey were searched for systematic reviews, clinical trials, guidelines, other reports, reviews, efficacy and safety information. As per the hierarchy of evidence, high quality systematic reviews and evidence based guidelines were searched for first, followed by phase 3 randomized controlled trials, etc.

Long-acting opioids & recent FDA approvals

Appendix 1 contains a drug summary table containing information on the long-acting (LA) opioids. These LA opioids (apart from Xartemis XR) are indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options (such as non-opioid analgesics or immediate-release opioids), are either inadequate, ineffective, or not tolerated.²¹⁻²³ Xartemis XR has a bilayer formulation (immediate and extended-release) and contains oxycodone and acetaminophen (maximum of 4000 mg acetaminophen/day recommended by manufacturer).²³ It is indicated in the management of acute pain (vs. other LA opioids that are indicated for long-term opioid treatment) severe enough to require opioid treatment and for which alternative treatment options are inadequate.^{22,23} XARTEMIS XR was approved by the FDA in March 2014, and was not formulated as an abuse-deterrent product.^{23,24}

A number of LA opioid formulations have been approved by the FDA in the last 2 years and these products were specifically formulated as abuse-deterrent. In November 2014, the FDA approved Hysingla ER (24-hour hydrocodone ER tablet), and in January 2015, the reformulated Zohydro ER (12-hour hydrocodone ER capsule). In April 2016, the FDA approved XTAMPZA ER (oxycodone) extended-release oral capsules (CII).⁹

It is important to note that all these LA opioid products can be abused and are subject to misuse, addiction, and criminal diversion, and the high drug content in extended-release formulations adds to the risk of adverse outcomes from abuse and misuse.⁹

The abuse-deterrent formulations are intended to hopefully prevent these problems, but abuse and misuse is still possible. XTAMPZA ER capsules for example contain microspheres formulated with inactive ingredients

that has been shown to make abuse by injection difficult, and are expected to reduce abuse via the intranasal route (in vitro data, pharmacokinetic and human abuse potential studies), but additional data in the future would provide a better understanding of its abuse potential. “Abuse of XTAMPZA ER by injection and by the nasal route of administration, as well as by the oral route is still possible.”⁹

All these LA opioid products included in this report are classified as Schedule II controlled substances by the FDA.^{22,23}

Methadone

Methadone is a pharmacologically long-acting opioid (others are pharmaceutically manipulated ER/LA formulations). It has pharmacokinetic and pharmacodynamic properties that distinguish it from other opioids.²⁵ Use of methadone in the management of pain has been increasing due to some desirable properties, but it also has some less desirable characteristics.²⁶ In the US, rates of methadone use for pain, methadone prescriptions and methadone-related overdose deaths have been rising, and the majority of these deaths appear to be related to the rise in the use of methadone in chronic pain.^{27,28} “More than 30% of prescription analgesic deaths in the United States involve methadone, even though methadone prescribing accounts for a relatively small share, 2%, of analgesic prescriptions.”^{25,29}

Table 1. Methadone characteristics²⁵⁻²⁷

Positive/advantageous	Less desirable (vs. other opioids)
High oral bioavailability (Most opioids have less than 40% oral bioavailability)	Highly variable inter-individual pharmacokinetics
Rapid onset of analgesic effect	High potential for accumulation: <ul style="list-style-type: none"> ⇒ delayed toxicity including respiratory depression ⇒ may take up to 10 days to reach steady-state serum levels.
Long bi-phasic half-life (less frequent dosing schedules)	Potential drug interactions
Lack of active metabolites	Associated with QT prolongation/cardiac arrhythmias (especially at higher doses and with other QT-prolonging drugs)
Low cost (compared to other opioids that are pharmaceutically manipulated into controlled-release formulations).	Higher overdose incidence and mortality (1 of every 3 opioid-related deaths is associated with methadone ingestion) ^{28,30}

This review does not include methadone use in opioid addiction treatment, but includes information on use in pain management including pain management in patients enrolled in methadone maintenance treatment programs. Chronic pain is reported to be common in these patients (prevalence ranging between 37-60%)^{26,31-33}, but their pain could be inadequately managed due to physician concerns (e.g. prescription drug diversion, withdrawal symptoms with opioid cessation, adverse effects risks) and the belief that methadone treatment for addiction provides adequate pain relief.^{26,34,35}

- Currently, methadone is non-preferred on the Utah Medicaid Preferred Drug List (PDL).
- Methadone also has a clinical Prior Authorization (PA)

Factors to consider regarding appropriate long-acting opioid use

In addition to the factors to consider regarding opioid use that were discussed in the short-acting opioids for chronic non-cancer pain report (opioid tolerance; opioid sharing, storage and disposing of opioid medications, repeated dose escalations), “end of dose pain” should also be considered.

“End-of-dose pain” in chronic pain

Zimmerman and Richarz report that a large percentage of patients with chronic pain on around-the-clock (ATC) opioids may experience increased pain occurring at the end of a scheduled dose. Please refer to the systematic review section for information on this phenomenon and LA vs SA opioids.³⁶

Clinical Guidelines and related evidence

Note that this contains similar information to what was included in the short-acting opioid report, but guidelines were reviewed again for long-acting opioid information. Additional information was added to this section. Please note that this is a brief summary of some of the information in these guidelines. Please refer to the guidelines for complete information.

Table 2. Guidelines

CDC Guideline for Prescribing Opioids for Chronic Pain - United States, 2016.^{13,37}

“OBJECTIVE: To provide recommendations about opioid prescribing for primary care clinicians treating adult patients with chronic pain outside of active cancer treatment, palliative care, and end-of-life care.”

1) when to initiate or continue opioids for chronic pain; 2) opioid selection, dosage, duration, follow-up, and discontinuation; and 3) assessing risk and addressing harms of opioid use.

This is just a summary of some of the recommendations. Please refer to guidelines for all 12 recommendations.

- Treatment of chronic pain: non-opioid therapy is preferred
- “Opioids should be used only when benefits for pain and function are expected to outweigh risks.”
- Immediate-release opioids should be prescribed instead of LA/ER opioids when starting opioid therapy for pain.
- “When opioids are started, clinicians should prescribe the lowest effective dosage. Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when increasing dosage to 50 morphine milligram equivalents (MME) or more per day, and should avoid increasing dosage to 90 MME or more per day or carefully justify a decision to titrate dosage to 90 MME or more per day.”¹³
- The lowest effective dose of IR opioids should be prescribed.
- Only the quantity needed for the expected duration of pain severe enough to require opioids should be prescribed. “Three days or less will often be sufficient; more than 7 days will rarely be needed.”
- “Clinicians should evaluate benefits and harms with patient within 1 to 4 weeks starting opioid therapy for chronic pain or dose escalation.”
- “Clinicians should evaluate benefits and harms of continued opioid therapy with patients every 3 months or more frequently and review prescription drug monitoring program data, when available, for high-risk combinations or dosages.”
- Higher opioid dosages (≥50 MME/d) is one of the risk factors that clinicians need to evaluate for opioid-related harm/overdose (also, history of overdose or substance use disorder) and for which strategies to mitigate risk into the management plan needs to be incorporated.
- State prescription drug monitoring data should be reviewed by clinicians
- Avoid concurrent opioids and benzodiazepines whenever possible.
- Treatment should be offered to patients with opioid use disorder.

2012 American College of Emergency Physicians

Clinical policy: critical issues in the prescribing of opioids for adult patients in the emergency department.

“Major Recommendations

1. In the adult Emergency Department (ED) patient with noncancer pain for whom opioid prescriptions are considered, what is the utility of state prescription drug monitoring programs in identifying patients who are at high risk for opioid abuse?

Level A recommendations. None specified.

Level B recommendations. None specified.

Level C recommendations. The use of a state prescription monitoring program may help identify patients who are at high risk for prescription opioid diversion or doctor shopping.

2. In the adult ED patient with acute low back pain, are prescriptions for opioids more effective during the acute phase than other medications?

Level A recommendations. None specified.

Level B recommendations. None specified.

Level C recommendations.

1. For the patient being discharged from the ED with acute low back pain, the emergency physician should ascertain whether nonopioid analgesics and nonpharmacologic therapies will be adequate for initial pain management.
 2. Given a lack of demonstrated evidence of superior efficacy of either opioid or nonopioid analgesics and the individual and community risks associated with opioid use, misuse, and abuse, opioids should be reserved for more severe pain or pain refractory to other analgesics rather than routinely prescribed.
 3. If opioids are indicated, the prescription should be for the lowest practical dose for a limited duration (e.g., <1 week), and the prescriber should consider the patient’s risk for opioid misuse, abuse, or diversion.
3. In the adult ED patient for whom opioid prescription is considered appropriate for treatment of new-onset acute pain, are short-acting schedule II opioids more effective than short-acting schedule III opioids?

Level A recommendations. None specified.

Level B recommendations. For the short-term relief of acute musculoskeletal pain, emergency physicians may prescribe short-acting opioids such as oxycodone or hydrocodone products while considering the benefits and risks for the individual patient.

Level C recommendations. Research evidence to support superior pain relief for short-acting schedule II over schedule III opioids is inadequate.

4. In the adult ED patient with an acute exacerbation of noncancer chronic pain, do the benefits of prescribing opioids on discharge from the ED outweigh the potential harms?

Level A recommendations. None specified.

Level B recommendations. None specified.

Level C recommendations.

1. Physicians should avoid the routine prescribing of outpatient opioids for a patient with an acute exacerbation of chronic noncancer pain seen in the ED.
2. If opioids are prescribed on discharge, the prescription should be for the lowest practical dose for a limited duration (e.g., <1 week), and the prescriber should consider the patient’s risk for opioid misuse, abuse, or diversion.

The clinician should, if practicable, honor existing patient-physician pain contracts/treatment agreements and consider past prescription patterns from information sources such as prescription drug monitoring programs.”

2012 American Society of Interventional Pain Physicians (ASIPP) guidelines for responsible opioid prescribing in chronic non-cancer pain: Part I—evidence assessment.³⁸

“1) There is good evidence that non-medical use of opioids is extensive; one-third of chronic pain patients may not use prescribed opioids as prescribed or may abuse them, and illicit drug use is significantly higher in these patients.

2) There is good evidence that opioid prescriptions are increasing rapidly, as the majority of prescriptions are from non-pain physicians, many patients are on long-acting opioids, and many patients are provided with combinations of long-acting and short-acting opioids.

3) There is good evidence that the increased supply of opioids, use of high dose opioids, doctor shoppers, and patients with multiple comorbid factors contribute to the majority of the fatalities.

4) There is fair evidence that long-acting opioids and a combination of long-acting and short-acting opioids contribute to increasing fatalities and that even low-doses of 40 mg or 50 mg of daily morphine equivalent doses may be responsible for emergency room admissions with overdoses and deaths.

5) There is good evidence that approximately 60% of fatalities originate from opioids prescribed within the guidelines, with approximately 40% of fatalities occurring in 10% of drug abusers.

6) The short-term effectiveness of opioids is fair, whereas the long-term effectiveness of opioids is limited due to a lack of long-term (> 3 months) high quality studies, with fair evidence with no significant difference between long-acting and short-acting opioids.

7) Among the individual drugs, most opioids have fair evidence for short-term and limited evidence for long-term due to a lack of quality studies.

8) The evidence for the effectiveness and safety of chronic opioid therapy in the elderly for chronic non-cancer pain is fair for short-term and limited for long-term due to lack of high quality studies; limited in children and adolescents and patients with comorbid psychological disorders due to lack of quality studies; and the evidence is poor in pregnant women.

9) There is limited evidence for reliability and accuracy of screening tests for opioid abuse due to lack of high quality studies.

10) There is fair evidence to support the identification of patients who are non-compliant or abusing prescription drugs or illicit drugs through urine drug testing and prescription drug monitoring programs, both of which can reduce prescription drug abuse or doctor shopping."

2012 American Society of Interventional Pain Physicians (ASIPP) guidelines for responsible prescribing in chronic non-cancer pain: part 2 – guidance³⁹

"Part 2 of the guidelines on responsible opioid prescribing provides the following recommendations for initiating and maintaining chronic opioid therapy of 90 days or longer."³⁹

- Establishing diagnosis: "A pain management consultation, for non-pain physicians, if high-dose opioid therapy is being utilized. (Evidence: fair)"
- "The long-acting opioids in high doses are recommended only in specific circumstances with severe intractable pain that is not amenable to short-acting or moderate doses of long-acting opioids, as there is no significant difference between long-acting and short-acting opioids for their effectiveness or adverse effects. (Evidence: fair)"
- "A trial of opioid rotation may be considered for patients requiring escalating doses. (Evidence: limited)"
- "Once medical necessity is established, opioid therapy may be initiated with low doses and short-acting drugs with appropriate monitoring to provide effective relief and avoid side effects. (Evidence: fair for short-term effectiveness, limited for long-term effectiveness)"
- "Up to 40 mg of morphine equivalent doses are being recommended as low dose, 41 to 90 mg of morphine equivalent dose as a moderate dose, and greater than 91 mg of morphine equivalence as high doses. (Evidence: fair)"
- "In reference to long-acting opioids, titration must be carried out with caution and overdose and misuse must be avoided. (Evidence: good)"
- "Methadone is recommended for use in late stages after failure of other opioid therapy and only by clinicians with specific training in the risks and uses. (Evidence: limited)"

Adherence Monitoring

1. "Monitoring recommendation for methadone prescription is that an electrocardiogram should be obtained prior to initiation, at 30 days and yearly thereafter. (Evidence: fair)"
2. In order to reduce prescription drug abuse and doctor shopping, adherence monitoring by urine drug testing and PMDPs provide evidence that is essential to the identification of those patients who are non-compliant or abusing prescription drugs or illicit drugs. (Evidence: fair)"

2009 Clinical Guidelines from the American Pain Society and the American Academy of Pain Medicine on the use of chronic opioid therapy in chronic noncancer pain¹⁵

Please refer to the guideline for all recommendations. This is just the section regarding dosage and some additional information.

Dose escalations and high dose opioids

"Theoretically, opioids have no maximum or ceiling dose. In practice, progressively higher opioid doses may improve symptom control in some patients, but can also result in additional adverse effects with little incremental benefit, or be a marker for substance abuse or diversion. The guideline defines high dose opioid therapy as >200 mg daily of oral morphine (or equivalent).⁴⁰

These doses are outside the ranges evaluated in randomized trials and prescribed in only a small minority of patients in observational studies.⁴¹⁻⁴³ When opioid doses reach this threshold, more frequent and intense monitoring is recommended. Clinicians should consider weaning or discontinuation of chronic opioid therapy if assessments indicate reduced analgesia, function, or quality of life; aberrant drug-related behaviors; or the presence of intolerable adverse effects."¹⁵

Some additional information:

Initiation and titration of chronic opioid therapy

"Clinicians and patients should regard initial treatment with opioids as a therapeutic trial to determine whether chronic opioid therapy is appropriate (strong recommendation, low-quality evidence)."

"Opioid selection, initial dosing, and titration should be individualized according to the patient's health status, previous exposure to opioids, attainment of therapeutic goals, and predicted or observed harms (strong recommendation, low-quality evidence).

There is insufficient evidence to recommend short-acting versus long-acting opioids, or as-needed versus around-the-clock dosing of opioids."

Methadone

"Methadone is characterized by complicated and variable pharmacokinetics and pharmacodynamics and should be initiated and titrated cautiously, by clinicians familiar with its use and risks (strong recommendation, moderate-quality evidence)."

Dose escalations and high-dose therapy

“When repeated dose escalations occur in patients on chronic opioid therapy, clinicians should evaluate potential causes and re-assess benefits relative to harms (strong recommendation, low-quality evidence).”

“In patients who require relatively high doses of chronic opioid therapy clinicians should evaluate for unique opioid-related adverse effects, changes in health status, and adherence to the chronic opioid therapy treatment plan on an ongoing basis, and consider more frequent follow-up visits (strong recommendation, low-quality evidence).”

Opioid rotation

“Clinicians should consider opioid rotation when patients on chronic opioid therapy experience intolerable adverse effects or inadequate benefit despite dose increases (weak recommendation, low-quality evidence).”

Identifying a medical home and when to obtain consultation

“Patients on chronic opioid therapy should identify a clinician who accepts primary responsibility for their overall medical care. This clinician may or may not prescribe chronic opioid therapy, but should coordinate consultation and communication among all clinicians involved in the patient’s care (strong recommendation, low-quality evidence).”

“Clinicians should pursue consultation, including interdisciplinary pain management, when patients with chronic noncancer pain may benefit from additional skills or resources that they cannot provide (strong recommendation, moderate-quality evidence).”

2010 Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-Cancer Pain¹⁴

≥200 mg/day MED is considered a “watchful dose”

“Chronic non-cancer pain can be managed effectively in most patients with dosages at or below 200 mg/day of morphine or equivalent (Grade A). Consideration of a higher dosage requires careful reassessment of the pain and of risk for misuse, and frequent monitoring with evidence of improved patient outcomes (Grade C).”¹⁴

NICE guidelines [CG173] Neuropathic pain in adults: pharmacological management in non-specialist settings⁴⁴

Published date: November 2013 Last updated: December 2014

Treatment

- For **all neuropathic pain (except trigeminal neuralgia)** offering a choice of amitriptyline, duloxetine, gabapentin or pregabalin as initial treatment is suggested (If the initial treatment is not effective or is not tolerated, offer one of the remaining 3 drugs, and consider switching again if the second and third drugs tried are also not effective or not tolerated).
- “Consider tramadol only if acute rescue therapy is needed (see recommendation below about long-term use).”
- “Consider capsaicin cream for people with localised neuropathic pain who wish to avoid, or who cannot tolerate, oral treatments.”

Treatments that should not be used

“Do not start the following to treat neuropathic pain in non-specialist settings, unless advised by a specialist to do so:

- cannabis sativa extract
- capsaicin patch
- lacosamide
- lamotrigine
- levetiracetam
- morphine
- oxcarbazepine
- topiramate
- tramadol (this is referring to long-term use; see recommendation above for short-term use)
- venlafaxine.”

Trigeminal neuralgia

- “Offer carbamazepine as initial treatment for trigeminal neuralgia.
- If initial treatment with carbamazepine is not effective, is not tolerated or is contraindicated, consider seeking expert advice from a specialist and consider early referral to a specialist pain service or a condition-specific service.”

Pan Birmingham Cancer Network NHS Guidelines for the use of Methadone for Adults with Pain in Palliative Care⁴⁵

Date approved by Network Governance: October 2012

Given that there are no NICE guidelines regarding the use of methadone for pain, information from this group was included as it provides useful information.

Guideline Background

- “2.1 There are no NICE guidelines on the use of methadone for pain therefore the Pan Birmingham Cancer Network Specialist Palliative Audit and Guidelines Group have developed these guidelines to ensure safe and consistent practice in-line with local expert opinion.
- 2.2 A small number of patients with cancer experience pain that cannot be controlled using the analgesic ladder even when anti-epileptics and anti-depressant drugs are added to opiates¹. Methadone may help in the pain management of these patients.
- 2.3 Methadone has a long half-life and titration to an effective dose is often complex therefore dose titration and modification should be carried out under the care and supervision of a specialist palliative care or pain team.”⁴⁵

Guideline Statements

- “3.1 The use of methadone for analgesia requires the involvement of the specialist palliative care team at all stages.
- 3.2 Patients with uncontrolled pain should be referred either to a specialist palliative care or a pain team.
- 3.3 The use of methadone should be reserved for the management of pain in patients that:
- a. gain inadequate analgesia with or without unacceptable side effects following appropriate dose-escalation of morphine and/or other opioids
 - b. experience tolerance to the analgesic effects of other opioids
 - c. are receiving methadone for another indication
- 3.4 Conversion to methadone requires careful monitoring and where possible should take place in a specialist palliative care in-patient unit. Under exceptional circumstances with the involvement of the specialist palliative care or pain team the conversion may occasionally be undertaken at home or in another care environment.
- 3.5 Consideration should be made of the risk of long QT syndrome
- 3.6 Methadone prescribing responsibilities should only be passed onto the primary care team when the patient has been stabilised and with the support of shared care guidelines and in the areas where shared care has been approved.
- 3.7 Conversion from other opioids to sub-cutaneous methadone:
- 3.7.1 It is not advised to convert to sub-cutaneous methadone from any opioid other than oral methadone and is not covered by this guideline.
- 3.7.2 Conversion is a prolonged process requiring considerable input from the patient to achieve successful conversion to oral methadone, so changing a patient in the final few days of life to sub-cutaneous methadone from other opioids is not advised.”⁴⁵

Management of Breakthrough Pain

- “5.1 For patients in severe pain and requiring analgesia within the 3 hour interval between methadone doses, options are:
- Taking the previously used opioid (at 50-100% of the prn dose before switching) with a minimum of hourly intervals.
 - If neurotoxicity with pre-switch opioid then use an appropriate dose of an alternative strong opioid.”⁴⁵

2014 Methadone Safety: A Clinical Practice Guideline From the American Pain Society and College on Problems of Drug Dependence, in Collaboration With the Heart Rhythm Society²⁸

“Although these guidelines are based on a systematic review, the panel identified numerous research gaps, most recommendations were based on low-quality evidence, and no recommendations were based on high-quality evidence. PERSPECTIVE: This guideline, based on a systematic review of the evidence on methadone safety, provides recommendations developed by a multidisciplinary expert panel. Safe use of methadone requires clinical skills and knowledge in use of methadone to mitigate potential risks, including serious risks related to risk of overdose and cardiac arrhythmias.”²⁸

“Patient Assessment and Selection

When considering initiation of methadone, the panel recommends that clinicians perform an individualized medical and behavioral risk evaluation to assess risks and benefits of methadone, given methadone's specific pharmacologic properties and adverse effect profile (strong recommendation, low-quality evidence).

Patient Education and Counseling

The panel recommends that clinicians educate and counsel patients prior to the first prescription of methadone about the indications for treatment and goals of therapy, availability of alternative therapies, and specific plans for monitoring therapy, adjusting doses, potential adverse effects associated with methadone, and methods for reducing the risk of potential adverse

effects and managing them (strong recommendation, low-quality evidence).

Baseline Electrocardiograms

- The panel recommends that clinicians *obtain* an electrocardiogram (ECG) prior to initiation of methadone in patients with risk factors for corrected electrocardiographic QT (QTc) interval prolongation, any prior ECG demonstrating a QTc >450 ms, or a history suggestive of prior ventricular arrhythmia. An ECG within the past 3 months with a QTc <450 ms in patients without new risk factors for QTc interval prolongation can be used for the baseline study (strong recommendation, low-quality evidence).
- The panel recommends that clinicians *consider* obtaining an ECG prior to initiation of methadone in patients not known to be at higher risk for QTc interval prolongation; an ECG within the past year with a QTc <450 ms in patients without new risk factors for QTc interval prolongation can be used for the baseline study (weak recommendation, low-quality evidence).
- The panel recommends against use of methadone in patients with a baseline QTc interval >500 ms (strong recommendation, low-quality evidence).
- The panel recommends that clinicians consider alternate opioids in patients with a baseline QTc interval ≥450 ms but <500 ms. If methadone is considered in a patient with a baseline QTc interval ≥450 ms but <500 ms, the clinician should evaluate for and correct reversible causes of QTc interval prolongation before initiating methadone (weak recommendation, low-quality evidence).
- The panel recommends that clinicians consider buprenorphine as a treatment option for patients treated for opioid addiction who have risk factors for or known QTc interval prolongation when an agonist/partial agonist is indicated (weak recommendation, moderate-quality evidence).

Initiation of Methadone

The panel recommends that clinicians initiate methadone at low doses individualized based on the indication for treatment and prior opioid exposure status, titrate doses slowly, and monitor patients for sedation (strong recommendation, moderate-quality evidence).

Practice Advice: Based on limited research evidence and clinical experience, the panel suggests the following parameters:

1. When used to treat opioid addiction, the panel suggests that clinicians start methadone at no more than 30 to 40 mg once daily. The dose should be titrated based on objective signs of withdrawal and self-reported craving and methadone dose increased by no more than 10 mg/d and no more frequently than every 3 to 4 days. Methadone should be withheld if there is evidence of sedation.
2. When used to treat chronic pain in adults on relatively low doses of other opioids (e.g., <40 to 60 mg/d of morphine or equivalent), the panel suggests that clinicians start methadone at 2.5 mg three times a day (tid), with initial dose increases of no more than 5 mg/d every 5 to 7 days. In children, the recommended starting dose is 100 µg/kg (maximum 5 mg/dose) every 6 to 8 hours. Methadone should be withheld if there is evidence of sedation.
3. When used to treat chronic pain and switching to methadone from higher doses of another opioid, the panel suggests that clinicians start methadone therapy at a dose 75% to 90% less than the calculated equianalgesic dose and at no higher than 30 to 40 mg/d, with initial dose increases of no more than 10 mg/d every 5 to 7 days. Methadone should be withheld if there is evidence of sedation.

The panel recommends that clinicians consider those patients previously prescribed methadone, but who have not currently taken opioids for 1 to 2 weeks, opioid-naïve for the purpose of methadone reinitiation (strong recommendation, low-quality evidence).

Follow-up Electrocardiograms

- The panel recommends that for patients prescribed methadone, clinicians perform follow-up ECGs based on baseline ECG findings, methadone dose changes, and other risk factors for QTc interval prolongation (strong recommendation, low-quality evidence).

Practice Advice: Based on limited research evidence and based upon clinical experience, the panel suggests the following parameters:

1. The panel suggests that for patients with risk factors for QTc interval prolongation, any prior ECG demonstrating a QTc >450 ms, or a history of syncope, clinicians perform follow-up ECG 2 to 4 weeks after initiation of methadone therapy and following significant dose increases.
 2. The panel suggests that for all patients, clinicians perform follow-up ECG when the methadone dose reaches 30 to 40 mg/d in patients started at lower doses, and again at 100 mg/d.
 3. The panel suggests that clinicians perform follow-up ECG for all patients prescribed methadone with new risk factors for QTc interval prolongation or signs or symptoms suggesting arrhythmia.
- The panel recommends that clinicians switch methadone-treated adults with a QTc interval ≥500 ms to an alternative opioid or immediately reduce the methadone dose; in all such cases, the panel recommends that clinicians evaluate and correct reversible causes of QTc interval prolongation, and repeat the ECG after the methadone dose has been decreased (strong recommendation, low-quality evidence).
 - The panel recommends that clinicians consider switching methadone-treated adults with a QTc interval ≥450 ms but <500 ms to an alternative opioid or reducing the methadone dose. In patients in whom there are barriers to switching to

alternative opioids, or who experience decreased treatment effectiveness with methadone dose reductions, the panel recommends that clinicians discuss with patients the potential risks of continued methadone. In all cases, the panel recommends that clinicians evaluate and correct reversible causes of QTc interval prolongation, and repeat the ECG after the methadone dose has been decreased (strong recommendation, low-quality evidence).

Monitoring for and Management of Adverse Events

- The panel recommends that patients receiving methadone be monitored for common opioid adverse effects and toxicities and that adverse effects management be considered part of routine therapy (strong recommendation, moderate-quality evidence).
- The panel recommends face-to-face or phone assessment with patients to assess for adverse events within 3 to 5 days after initiating methadone, and within 3 to 5 days after each dose increase (strong recommendation, low-quality evidence).

Urine Drug Testing

- The panel recommends that clinicians obtain urine drug screens prior to initiating methadone and at regular intervals in patients prescribed methadone for opioid addiction (strong recommendation, low-quality evidence).
- The panel recommends that patients prescribed methadone for chronic pain who have risk factors for drug abuse undergo urine drug testing prior to initiating methadone and at regular intervals thereafter; it recommends that clinicians consider urine drug testing in all patients regardless of assessed risk status (strong recommendation, low-quality evidence).

Medication Interactions

The panel recommends that clinicians use methadone with care in patients using concomitant medications with potentially additive side effects or pharmacokinetic or pharmacodynamic interactions with methadone (strong recommendation, low-quality evidence).

Methadone Use in Pregnancy

The panel recommends monitoring of neonates born to mothers receiving methadone for neonatal abstinence syndrome and treatment for neonatal abstinence syndrome when present (strong recommendation, moderate-quality evidence).²⁸

The Methadone Safety guidelines: A Live Webinar Q&A (November 11, 2014)⁴⁶

Several questions were submitted to Chou and Wimer (Oregon Health Sciences University). Only some of those thought to be relevant to this report and decision-process are discussed here. Please refer to the original document for all questions and answers.

Question regarding breakthrough pain and percent of long acting opioids:

“According to the FDA, Methadone HCl is included in the list of Long Acting Opioid Medications.” The question was posed whether there is a guideline as to what medications are best if a breakthrough medication is considered and what percent of the total opioid should be appropriate when using methadone as the long-acting medication. “Several mail order pharmacies require that the long-acting medication be no less than 80% of the total morphine equivalent dose.”

Answer:

“There is very little data to guide use of breakthrough opioids in patients on long-acting opioids. Short-acting opioids are recommended for management of acute pain including breakthrough pain. We are not aware of any evidence-based rationale for requiring 80% of the total morphine-equivalent dose (MED) to be long-acting opioid.”

Question regarding conversion (methadone to other opioids):

Answer:

As discussed previously, the limitations of conversion ratios are also mentioned in their response.

“There is not a lot of evidence to guide switching from methadone to other opioids; however the conversion ratios are not thought to be bidirectional, there is potential incomplete cross-tolerance, there is high interindividual variability in dose conversion ratios, and conversions are complicated by the long half-life of methadone. We recommend very cautious conversion ratios (e.g., 7:1 or higher) with close monitoring; pharmacist assistance may be very helpful.”

Question regarding weaning methadone in a patient who is on methadone at MED of >1000, specifically patients with Sickle Cell Disease:

Answer:

“Unfortunately, there is no data to guide this; however, in general practice, I would recommend that you taper the patient by 5-10% every 1-2 weeks as long as there is no urgent need for the taper (i.e. somnolence, QTc prolongation >500ms, abuse or misuse, etc). If there is an urgent need for a taper, the patient may need to be admitted to the hospital to switch him or her to a more reasonable and safe pain regimen. Medications that can help with opioid withdrawal symptoms during a taper include clonidine, hydroxyzine, Tylenol or ibuprofen, hyocosamine, ondansetron or Phenergan, and fluids.”

Question regarding legality of prescribing methadone for chronic pain at a substance abuse inpatient treatment center (“does the provider need to be pain doctor or primary care provider”?)

“Legally, you can only prescribe methadone for the treatment of an opioid use disorder in an outpatient methadone maintenance program. That said, methadone dose typically provide at least 4-6 hours of analgesic benefit to patients in these programs. Inpatient treatment centers may allow their patients to be prescribed methadone for chronic pain in the absence of an opioid use disorder, but that would be up to the individual treatment center.”

Systematic Reviews

Please refer to the short-acting opioids in chronic non-cancer pain report for information regarding dosage or titration and opioid uses.

Systematic reviews – methadone or long-acting opioids

A search specifically for “methadone” or long-acting opioids were conducted in the Cochrane Library. Reviews that focused on opioid addiction treatment or cancer pain were excluded.

Cochrane Reviews

Methadone has different characteristics from other opioids.²⁵ Haroutiunian et al. (2012 Cochrane review) assessed the analgesic effectiveness and safety of methadone in the treatment of CNCP.²⁵ The authors concluded that *“The three studies provide very limited evidence of the efficacy of methadone for CNCP, and there were too few data for pooled analysis of efficacy or harm, or to have confidence in the results of the individual studies. No conclusions can be made regarding differences in efficacy or safety between methadone and placebo, other opioids, or other treatments.”*²⁵

Other Reviews (Cochrane Library that met the inclusion criteria for DARE)

Sandoval et al. (2005 Other review) reported on the effectiveness and side-effects of oral methadone for chronic noncancer pain.^{47,48} The maximum methadone dose ranged from 20 to 930 mg/day in the studies where it was reported.^{47,48} This review included only one small randomized controlled trial (RCT) (n=19) in which a “statistically significant well-defined analgesic effect was seen for 20 mg/day methadone compared with placebo (based on 11 patients), but not for a dose of 10 mg/day.”⁴⁷ 7 case series (n=495) and 13 case reports (n=31) were also included for which the authors categorized results into 3 arbitrary categories; “methadone was associated with 'meaningful' pain relief results in 59% of patients, 'non-meaningful' in 40% and 'unclassifiable' in 1%.”^{47,48} The Centre for Reviews and Dissemination stated that “the authors reported adequate details of each of the included studies, which highlighted clinical and methodological variation across the included studies.”^{47,48} Data on specific pain syndromes was lacking and in general the side-effects most frequently reported were considered minor.^{47,48} Due to the limited evidence available, the authors

concluded that “well-designed controlled studies are needed to provide more accurate information on the efficacy of methadone in pain syndromes, in particular neuropathic pain.”^{47,48}

*Comparative efficacy and safety of long-acting oral opioids for chronic non-cancer pain: a systematic review (Provisional abstract)*⁴⁹

In this 2003 review that included 16 RCTs (n=1427; none of good quality) and 8 observational studies (n=1190 for adverse events), Chou et al. evaluated and summarized the evidence for the comparative efficacy and safety of long-acting opioids in the management of chronic non-cancer pain.⁵⁰ The authors found that there was insufficient evidence to “to prove that different long-acting opioids are associated with different efficacy or safety profiles” and “to determine whether long-acting opioids as a class are more effective or safer than short-acting opioids.”⁵⁰ “A subgroup of three studies on long-acting versus short-acting oxycodone was more homogeneous and provided fair evidence that these formulations are equally effective for pain control.”⁵⁰

*End-of-dose pain in chronic pain: does it vary with the use of different long-acting opioids? (Provisional abstract)*⁵¹

In this 2015 review, Zimmerman and Richards explored how the frequency of end-of-dose pain is linked to the formulations of long-acting opioids. Breakthrough pain (BTP) was used as a surrogate parameter because they only found a few studies that mentioned end-of-dose pain explicitly.^{36,51}

*“Of the 39 studies entered in the final analysis, 14 studies across different formulations showed that ER opioids were effective in the prevention of BTP. The opioids most frequently studied were hydromorphone (26%), followed by morphine (23%), and transdermal buprenorphine (23%). Only 5% of the studies used immediate-release preparations. Overall, most studies showed that patients using ER preparations experienced fewer episodes of BTP compared with patients on placebo or an active comparator. This could reflect the favorable duration of action of these opioids compared with short-acting formulations.”*³⁶

The authors suggest that “future studies should examine the incidence of end-of-dose pain and use of rescue medicine in a longitudinal manner in patients with chronic pain taking short- vs. long-acting ATC opioids.”³⁶

*Impact of opioid rescue medication for breakthrough pain on the efficacy and tolerability of long-acting opioids in patients with chronic non-malignant pain (Structured abstract)*⁵²

Devulder et al. assessed the impact of opioid rescue medication on the effectiveness and tolerability of chronic opioid therapy for chronic non-malignant pain and concluded that “the evidence did not suggest that rescue medication with short-acting opioids for breakthrough pain affected analgesic efficacy or the incidence of adverse effects among patients receiving long-acting opioids for chronic non-malignant pain. However, further research is needed.”^{52,53} The CRD comments included several limitations which should be considered when interpreting the findings such as only 2 databases searched, publication and language biases, inappropriate tool used for validity assessment, *the use of rescue medication in the included studies was not quantified, studies may have been of too short duration to show an effect, and that outcome measures were relatively crude, analysis was based on untested assumptions and/or used data that had been manipulated by the reviewers, and indirect comparisons (which has its limitations).*⁵²

The CRD structured abstract include the following statement for implications of the review for practice and research:

*“Practice: The authors stated that use of short-acting immediate release opioids for breakthrough pain among patients with chronic non-malignant pain treated with long-acting opioids conferred no additional analgesic benefit, but did not reduce analgesic efficacy. Research: The authors stated that a RCT was required to assess the effects of long-term treatment with a long-acting opioid with or without opioid rescue medication among patients with chronic non-malignant pain.”*⁵²

Technology Assessments (Cochrane Library)

In a 2009 Canadian Agency for Drugs and Technologies in Health technology assessment, the evidence and guidelines assessing methadone dosing for the management of pain in opioid addicted patients was assessed.²⁶ It was questioned whether a maximum allowable dose for methadone should be established for managing pain in patients with a history of opioid addiction.²⁶

Authors' conclusions

“No information was identified from studies or guidelines to support a defined maximum daily dose for methadone when used for the management of pain in patients with a history of opioid addiction. Results from observational studies indicate that the optimal analgesic dose of methadone varies widely among participants when titrated according to analgesic effect and can be significantly higher than the maximum dose recommended for methadone maintenance treatment of opioid addiction. Current guidelines indicate that individuals receiving doses of methadone greater than 120 mg per day should be monitored for cardiac arrhythmias and other adverse effects. Further studies are needed to establish dosing recommendations and long-term feasibility of methadone treatment. In conclusion, dosing and administration of methadone for the management of pain in patients with a history of opioid addiction, including those enrolled in MMTPs, should be individualized and take into account the nature and severity of pain, degree of tolerance to the analgesic effects of methadone, and risk factors for adverse effects including cardiac arrhythmias and respiratory depression.”²⁶

Long-acting or short-acting opioids for chronic non-cancer pain (long-term opioid treatment)

It is current practice to switch patients to LA opioids if benefits outweigh the risks and it is determined that chronic opioid treatment is required because they provide a more stable blood concentration (smoother pain control and less risk of side-effects) and convenient dosing (“lower risk of being psychologically tied to the thought of taking his/her medication throughout the day”).⁵⁴

Even though it is believed in general that LA opioids have advantages over SA opioids, current evidences do not appear to substantiate this either way in terms of effectiveness or adverse effects. Refer to review by Chou et al. included in the section above (*Comparative efficacy and safety of long-acting oral opioids for chronic non-cancer pain: a systematic review (Provisional abstract)*)⁴⁹ According to the 2012 American Society of Interventional Pain Physicians (ASIPP) guidelines for responsible prescribing in chronic non-cancer pain: part 2 – guidance “...there is no significant difference between long-acting and short-acting opioids for their effectiveness or adverse effects.”³⁹ Doleys et al. state that the efficacy of opioids appear to be related to various other factors instead of only to pharmacodynamics or pharmacokinetic properties and lists examples such as age of patient and type of pain (nociceptive or neuropathic)⁵⁵, gender⁵⁶, history of substance abuse⁵⁷, cognitive functioning⁵⁸, and co-morbid psychopathology.^{11,59} Doleys et al. also discuss the roll that the patient’s perceived controllability of managing pain affects tolerance of pain.¹¹ The authors explored factors and outcomes in a small cohort of patients (50 patients) that have been using SA opioids for several years (keeping in mind that these patients were self-selected because they preferred SA opioids to previously trialed LA or were satisfied with the results of SA opioids and did not wish to change treatment, limiting generalizability; and limitation of self-reports e.g. recall and response bias).¹¹ “Most noteworthy is the degree of patient satisfaction, overall pain relief, and increased QoL, despite an estimated duration of pain relief of only 13.1 out of 24 hours.”¹¹ For some patients it is important to know that the opioid would work when needed i.e. the predictability and detectability of pain relief via use of short-acting opioids.¹¹ “This responsiveness to detectability may explain why some patients, even though they are taking substantial amounts of oral, transdermal, or intrathecal opioids, still seem to require or benefit from SA ‘breakthrough’

opioids.”¹¹ It is possible that there may be some patients that could benefit from SA opioid treatment, but more studies are needed to evaluate the safety and efficacy of chronic opioid therapy (long-acting and short-acting opioids). Also, further research is needed to explore factors affecting patient preference and responsiveness to certain opioids including the role of psychological and conditioning factors.

Safety

Several safety-related issues were discussed in the SA opioid report and will not be repeated in this section including:

- General safety information pertaining to all opioids
- The adverse effects/risks associated with higher doses
- The March 2016 FDA Opioid Pain Medicine Safety Alert regarding risks (including class-wide safety labeling changes regarding these)
- Moore et al. (Other review in Cochrane Library) stated that “there was no obvious relationship between the opioid type, dose or dosing regimen and the rate of adverse events”, and that “different painful conditions produced similar patterns of results.”⁶⁰ Refer to SA report for additional information and limitations.
- Dr Katz in a recent article in JAMA Internal Medicine entitled “Opioid Prescribing for Chronic Pain Not for the Faint of Heart”, said that when he prescribes opioids for chronic pain, he tries to keep the doses safe.⁶¹ *“When I prescribe opioids for chronic pain, I try to keep the doses safe. I only prescribe immediate-release opioids. I do not use extended-release or long-acting agents (recommendation 4). I do not prescribe methadone or fentanyl, and I do not prescribe in excess of 50 morphine milligram equivalents (MME)/d (recommendation 5). A typical pain prescription from me is 5 mg of hydrocodone with 325 mg of acetaminophen, 4 times a day as needed (50 mg of morphine = 50 mg of hydrocodone = 33 mg of oxycodone). I never prescribe more than a month of medication and never authorize refills. I think visits at least monthly are an important part of the assessment and treatment of chronic pain.”*⁶¹

The following FDA required warning is specifically related to ER opioid formulations and included in the product labels of all ER products:

*“Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with extended-release opioid formulations, reserve ‘opioid’ (specific opioid e.g. hydrocodone) ER for use in patients for whom alternative treatment options (eg, nonopioid analgesics, immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain. ‘Opioid’ ER is not indicated as an as-needed analgesic.”*²²

In 2010 and 2011 the FDA approved new crush-resistant formulations of OxyContin (oxycodone ER; reformulated) and Opana ER (oxymorphone).²³ The purpose of these formulations are to prevent the opioid medications from being cut, broken, chewed, crushed, or dissolved to release more medication that would hopefully lead to less abuse by snorting or injection and fewer overdoses, but more studies are needed to determine whether these formulations are subject to less misuse, abuse, diversion, overdose, or addiction.^{23,62} It can still be abused or misused by ingesting larger doses and quantity limitations could possibly help to prevent this to some extent.²³

It is also important to note the addition to the black box label regarding the risk of neonatal opioid withdrawal syndrome with prolonged use of ER opioids during pregnancy:

Prolonged use of ER opioid “can result in neonatal opioid withdrawal syndrome, which may be life-threatening if not recognized and treated, and requires management according to protocols developed by neonatology experts. If opioid use is required for a prolonged period in a pregnant woman, advise the patient of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available.”^{21,23}

Methadone:

It may take up to 5-7 days for plasma levels of methadone to stabilize so it is important to be cautious when titrating the methadone dose upward because toxicity may not become apparent immediately following a change in dosage (may take 5 days).⁶³ Due to its long half-life (8-12 hours after repeated dosing; initially 3-6 hours), it is not recommended to take methadone more frequently than every 8 hours.⁶³

The LA opioids have a FDA approved Risk Evaluation and Mitigation Strategy (REMS) requirement that consists of Medication Guides and Elements to Assure Safe Use.²¹ Manufacturers are required to make training available (regarding proper prescribing practices) and to educate patients and prescribers on the safe use of these products (educational material).²³

Long-acting opioids’ place in therapy and factors to consider

- **Chronic non-cancer pain & place in therapy:** Nonopioid therapy (refer to short-acting opioids in non-cancer pain report) and nonpharmacologic therapy are preferred to opioids because of the dangerous adverse effect profile of opioids.^{10,37} Opioids are not recommended for use in neuropathic pain, chronic back pain, chronic headaches, abdominal pain, or menstrual cramps.⁵⁴ For appropriate pain conditions in certain patients where it is determined that benefits outweigh the risks of opioid therapy IR opioids should be used when opioid therapy is initiated (instead of ER/LA opioids).³⁷ If a decision is made to continue opioid treatment long-term, short-acting or moderate doses of long-acting opioids should be considered (high dose LA are only for specific circumstances with severe intractable pain not responsive to SA or moderate doses of LA opioids).³⁹ Also, an informed assessment is needed to determine whether methadone may be an appropriate analgesic at this stage.²⁸ “Methadone is recommended for use in late stages after failure of other opioid therapy and only by clinicians with specific training in the risks and uses.”³⁹
- **Comparison of SA & LA:** “...there is no significant difference between long-acting and short-acting opioids for their effectiveness or adverse effects.”³⁹
- **Dose escalations:** “Repeated dose escalations can be a sign of substance abuse or diversion.” The 2012 American Society of Interventional Pain Physicians (ASIPP) guidelines for responsible prescribing in chronic non-cancer pain (part 2) guidance recommend that a trial of opioid rotation may be considered for patients requiring escalating doses.³⁹

The new CDC guidelines state that long-term opioid use often begins with treatment of acute pain, and therefore the following recommendations with regards to the lowest effective dose and duration of use have been made:

- **Dosage:** The lowest effective dose should be used. CDC guidelines: <50 MME/day³⁷, but several limitations (refer to tablet limitation section). Risk of overdose increases with increasing doses. As recommended in the 2012 American Society of Interventional Pain Physicians (ASIPP) guidelines, “A pain management consultation, for non-pain physicians, if high-dose opioid therapy is being utilized” may be good practice.³⁹
- **Duration of use/quantity:** Only the quantity that is needed for the expected duration of use. “Three days or less will often be sufficient; more than 7 days will rarely be needed.”³⁷ Excessive quantities increase

the risk for overdose and the risk of opioids being diverted and the risk of harming others. There is insufficient evidence for long-term use. Therefore, it would mainly be the SA opioids that should be used if it is determined that opioid therapy is needed. Long-term use should really only occur in some specific circumstances where there are no other options.

- **Titration:** Titration of LA opioids “must be carried out with caution and overdose and misuse must be avoided.”³⁹
- **Methadone monitoring:**
 - The 2012 American Society of Interventional Pain Physicians (ASIPP) guidelines for responsible prescribing in chronic non-cancer pain (part 2) guidance: “Monitoring recommendation for methadone prescription is that an electrocardiogram should be obtained prior to initiation, at 30 days and yearly thereafter.”³⁹
- **Dosage calculations/opioid conversion:** This was discussed extensively in the SA opioid report (Limitations of equianalgesic dose ratios/conversion factors e.g. variability and do not account for genetic factors, incomplete cross-tolerance, and pharmacokinetics).^{64,65} In addition it is important to note that Fudin states specifically with regards to methadone that it should be considered that “methadone prescriptions represent only 2% to 5% of all prescribed opioids, and yet methadone is involved in approximately 30% of all opioid deaths.”^{4,64} He speculates on potential reasons: “Is this because health care providers don’t know how to convert it? Or because of the drug’s long and variable half-life? Or because there are at least 6 cytochrome enzymes involved in its metabolism? Or because it depends on p-glycoprotein for absorption through the gut and into the central nervous system (CNS)? Or is it a combination of all of these?”⁶⁴ The significant and alarming variability in calculating morphine doses as found by 2 studies were discussed in the SA opioid report, and Fudin states: “Perhaps the most disturbing variation is the standard deviation values of fentanyl (\pm 136 mg) and methadone (\pm 122 mg).”^{64,66,67}
- The **January 2013 Centre for Medicare & Medicaid Services (CMS) bulletin** regarding “**Best Practices for Addressing Prescription Opioid Overdoses, Misuse and Addiction**”, provides examples of strategies that can be used to ensure appropriate use of opioid pain medications, and to help address the problem of opioid misuse and abuse.⁶⁸ These include “examples of methods states can use to target the prescribing of methadone for pain relief, given the disproportionate share of opioid-related overdose deaths associated with methadone when used as a pain reliever.”⁶⁸ *“Medicaid programs can encourage the use of safer, effective alternatives to opioid pain medications—in particular, alternatives to methadone prescribed for pain relief—by working collaboratively with other state agencies to educate Medicaid providers about opioid prescribing and dispensing practices. Medicaid programs can consider pharmacy benefit management strategies such as reassessing preferred drug list (PDL) placement, introducing clinical criteria, prior authorization, step therapy, quantity limits, and implementing drug utilization review (DUR) processes.”*⁶⁸
- **Prescriber education and quantity limitations:** Prescriber education is a valuable part of the process to combat this prescription opioid epidemic and would provide a better understanding of the Utah Medicaid planned initiative for opioid quantity limitations.
- **Challenges (as also described in SA opioid report):**
 - Patients already receiving high-dose opioids. Responsibility of physicians to communicate risks to patient and work with patient to lower dose to a safer level over time.⁶¹
 - Patients already receiving both benzodiazepines and opioids (should be avoided; CDC recommendations). Responsibility of physicians to communicate risks of overdose with patient and to discuss with other physician to determine whether both medications are really needed.⁶¹
 - Misuse/abuse/Potential diversion/selling medication or using other drugs (e.g. amphetamine, barbiturates, or cocaine) or multiple prescribers: Urine testing (CDC recommendation) may be useful in some patients if these are potential concerns.⁶¹ Also, the Utah Controlled Substance Database can provide useful information (CDC recommendation

regarding state's PMP). Wright et al. reported on a case where a patient with a history of alcohol and cocaine use disorders, and depression presented to the emergency department with suicidal ideation.⁶⁹ The state's prescription monitoring program revealed that the patient had received a 90- to 120-day supply of oxycodone and clonazepam every month for the last 7 months all from the same primary care physician and the prescriptions were found to be legitimate in the electronic health record (not photocopied prescriptions).⁶⁹ It was discovered that the patient would request a postdated prescription for the next month in addition to his prescription for that month every time when he visited the clinic to avoid difficulties of returning for a monthly visit.⁶⁹ "The physician added clear instructions for the pharmacist not to fill the second prescription until an exact date 30 days after the first prescription", but the postdated prescriptions were difficult to tract and the patient visited the clinic weeks earlier and asked for 2 prescriptions every time.⁶⁹ "Although the physician assumed that the pharmacy and insurer would prevent any early refills, the patient creatively used a number of small local pharmacies and paid out of pocket to avoid the restrictions imposed by his insurance plan. Because his primary care physician wrote all the prescriptions, the alerts for "doctor shoppers" in the state's monitoring program were not triggered."⁶⁹ Ensuring that the electronic health records is programmed to display the amount of medication prescribed during the last 30 days and alerts for early refills (at the time of prescribing) would help prescribers with this problem.⁶⁹ Monitoring the Controlled Substance Database would also prevent this from happening (especially when other prescribers are involved). However, medications obtained from someone else or street drugs would not be recorded in the controlled substance database.⁶¹

➤ Excessive prescribing leading to leftover medications which is an important source of opioids that are misused or diverted.^{19,20}

- **Special Populations:** It is important to consider that a large proportion of the Utah Medicaid population are pregnant women. Opioids are not recommended for use during pregnancy due to the associated adverse risks including premature births, spontaneous abortions, birth defects, neonatal abstinence syndrome (NAS), etc. and are only considered when all other options have been exhausted and the benefits outweigh the risk.⁵⁴
- **Age and gender:** Witkin et al. evaluated the influence of age and gender on opioid dosage in chronic noncancer pain clinic patients and found that males and patients aged 45-64 receive higher opioid doses than females and patients aged >=65.⁷⁰
- **Adverse effects/Safety:** Refer to safety section and appendix 1.
- **Therapeutic Duplication:** Use of 2 LA opioids e.g. methadone + ER morphine (MS Contin) should be questioned.⁶³ You may wish to consider limiting patients to one LA and one SA opioid agent.

- **Quantity limitations of some other plans** (identified through general internet search):

Table 3

Long-acting opioid	Health Plan of San Joaquin ⁵⁴ (Medi-Cal;SJHA) ^a	BlueCross BlueShield of Kansas ⁷¹ (document only covers Oxycodone ER)	PREMERA Blue Cross ⁷²	BlueCross BlueShield of North Carolina (PA for higher doses) ⁷³	Magellan Health Services TennCare ⁷⁴
Methadone (Dolophine)	–	–	–	5 mg: 180 per 30 days 10 mg: 360 per 30 days	5 mg: 8/day; 10 mg: 4/day; 5mg/5mL: 40mL/day; 10mg/5mL: 20mL/day; 10 mg/mL: 4mL/day
Morphine Sulfate ER tab (MS Contin)	3 per day	–	–	90 per 30 days	15, 30, 60mg:3/day; 100mg: 2/day; 200mg:1/day
Morphine Sulfate ER cap (Avinza) Discontinued ⁷⁵	NF; 1 per day (PA)	–	–	30 per 30 days	1/day
Morphine Sulfate ER cap (Kadian)	NF; 1 per day (PA)	–	–	–	130, 150, 200 mg: 1/day All other strengths: 2/day
Fentanyl (Duragesic Patch)	10 per 30 days	–	–	15 per 30 days	10 per 30 days
Oxycodone ER (OxyContin)	2 per day (PA)	10-40 mg: 2 per day 60 & 80 mg: 4 per day (PA for higher doses)	10-40 mg: 3 per day 60 & 80 mg tablets: 4 per day (PA for higher doses)	10-40 mg: 60 per 30 days 60&80 mg: 120 per 30 days	2/day (max: 1200mg oxycodone/30 days)
Hydrocodone ER (Zohydro ER; Hysingla ER)	–	–	60 per 30 days (PA for higher dose)	60 per 30 days	Hysingla: 1/day Zohydro: 2/day (max: 1200 mg hydrocodone/30 days)
Hydromorphone ER (Exalgo)	–	–	–	–	1/day
Oxymorphone ER (Opana ER tab)	–	–	–	60 per 30 days	2/day
Tapentadol ER (Nucynta ER tab)	–	–	–	60 per 30 days	2/day
Tramadol ER 100 mg, 200 mg, 300 mg	–	–	–	30 per 30 days	ConZip: 1/day

PA=Prior Authorization; NF=Non-formulary

a. Recommendations by the American Pain Society (APS), American Academy of Pain Medicine (AAPM), American Academy of Neurology (AAN), Veterans Affairs, the California Medical Board⁵⁴

- (no information): Information was not found in the particular document or reference regarding that product (does not mean they do not have a limitation in place; information could be in another document)

The San Joaquin opioid policy states that “For patients with chronic pain who require greater than 120 tablets per month, a long-acting opioid should be initiated (or increased) instead of exceeding 120 tablets per 30 days.⁵⁴ This policy states that they recognize that the definition of high-dose opioid therapy varies between different organizations, and they have chosen to adapt the cut-off of 120 mg MED/day as high dose opioid therapy (which they state is in alignment with Washington and Oregon State Opioid Prescribing Guidelines.⁵⁴ HPSJ also limits patients to one LA and one SA opioid at any given time.

MEDICAID

Table 4
Long-acting
opioid

	NYS Medicaid Fee-For-Service ⁷⁶	MassHealth ⁷⁷ January 2016 to go into effect on March 7, 2016 Updated high dose limit set at 120 mg/day of morphine equivalents	Oregon ⁷⁸ July 2016 Limit set at 90 MME per day and not to exceed quantity limits for Specific Opioid Products Subject to Quantity Limits per FDA-approved Labeling [Dose threshold]	Maryland ⁷⁹ July 2016 Comments: using FDA guidelines	Utah Medicaid Proposed Limit per month/30 days
Methadone (Dolophine)	12 units/day 360 units/30days	PA for all doses (new starters)	[20 mg/24 hours]	Dolophine all strengths & Diskets 40 mg dispersible tablets: 2 tabs/day	60 apart from 40mg which is 30
Morphine Sulfate ER tab (MS Contin)	15,30,60mg: 3 units/day, 90/30 days 100mg: 4 units per day, up to 3 times a day, max 120 units per 30 days. 200mg: max 2 units/day, max 60 units/30 days	MS Contin®, Oramorph SR® (morphine controlled release): dose limit 120 mg/day	[90 mg/24 hours]	MS Contin CR tablets all strengths: 2 tabs/day	90
Morphine Sulfate ER cap (Avinza) Discontinued ⁷⁵	–	morphine ER capsule: 1/day	[90 mg/24 hours]	1 cap/day	30
Morphine Sulfate ER cap (Kadian)	States Morphine ER excluding MS Contin so not sure whether for Kadian: 2 units/day; 60 units/30 days?	1 capsule/day	2 doses/day [90 mg/24 hours]	All strengths: 2 caps/day	60
Fentanyl (Duragesic Patch)	10 patches per 30 days; max 100mcg/hr (over a 72 hour dosing interval)	10 patches/month	1 dose/72 hours [37.5 mcg/hour q 72 hrs]	Fentanyl 37.5mcg/ 62.5mcg/ 87.5mcg/ patches & Duragesic patches (all strengths): 15 patches per 30 days	11
Oxycodone ER (OxyContin)	2 units/day; 60/30 days (not to exceed total daily dose of 160 mg)	3 tablets/day	2 doses/day [60 mg/24 hours]	2 tabs/day	60
ER capsules: Oxycodone hydrochloride 7.5 mg and acetaminophen 325 mg (Xartemis XR)	–	–	4 doses/day [60 mg/24 hours]	4 tabs/day	120
Oxycodone ER (Xtampza ER)	–	–	2 doses/day [60 mg/24 hours]	–	60
Hydrocodone ER (Zohydro ER; Hysingla ER)	Zohydro: 2 units /day; 60 units/30 days Hysingla: 1 unit/day; 30 units/30 days	Zohydro: 2 capsules/day Hysingla: 1 tablet/day	Zohydro: 2 doses/day Hysingla: 2 doses/day [90 mg/24 hours]	Zohydro: 2 caps/day Hysingla: 1 tab/day	60
Hydromorphone ER (Exalgo)	4 units / day (120 units/30 days)	1 tablet/day	1 dose/day [22.5 mg/24 hours]	1 tab/day	30
Oxymorphone ER (Opana ER tab)	4 units / day (120 units/30 days)	2 tablets/day	[30 mg/24 hours]	2 tabs/day	60

Long-acting opioid	NYS Medicaid Fee-For-Service ⁷⁶	MassHealth ⁷⁷	Oregon ⁷⁸	Maryland ⁷⁹	Utah Medicaid
		January 2016 to go into effect on March 7, 2016 Updated high dose limit set at 120 mg/day of morphine equivalents	July 2016 Limit set at 90 MME per day and not to exceed quantity limits for Specific Opioid Products Subject to Quantity Limits per FDA-approved Labeling [Dose threshold]	July 2016 Comments: using FDA guidelines	Proposed Limit per month/30 days

Tapentadol ER (Nucynta ER tab)	2 units/day (max of IR & ER should not exceed 500 mg/day)	–	[225 mg/24 hours]	2 tabs/day	60
Tramadol ER (Conzip, Ultram ER)	30 tabs/30 days	–	[300 mg/24 hours (ER)]	Conzip: 1 cap/day Ultram: 1 tab/day	30
Levorphanol (Levo-Dromoran)	–	2 tablets/day	–	–	Covered with SA opioids (60) Long duration of action Dosing 6-8 hrs Breakthrough pain, though may be useful as maintenance in some patients

Maryland uses FDA guidelines and clarifies what quantity limits include:

- “Dose efficiency edits – Limits coverage of prescriptions to one dose per day for drugs that are approved for once-daily dosing.
- Maximum daily dose – A message is sent to the pharmacy if a prescription is less than minimum or higher than the maximum allowed dose.
- Quantity limits over time – Limits coverage of prescriptions to a specific number of units in a defined amount of time.
- Dose optimization – For drugs whose different strengths all have the same or nearly the same unit cost, limits require using the highest possible strength rather than multiple units of lower strengths.”⁷⁹

Sickle Cell disease: Some plans mention that limits do not apply to patients with cancer or those with sickle cell disease e.g.

“Exemption for diagnosis of cancer or sickle cell disease.”⁷⁶

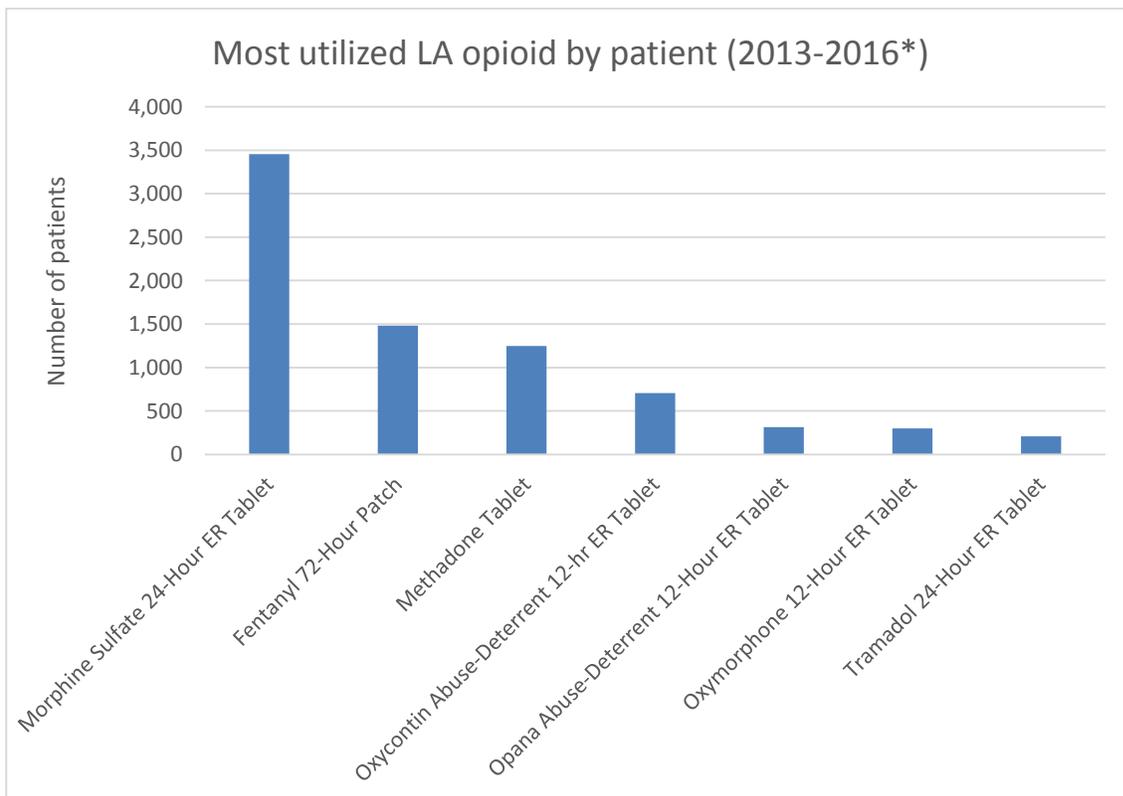
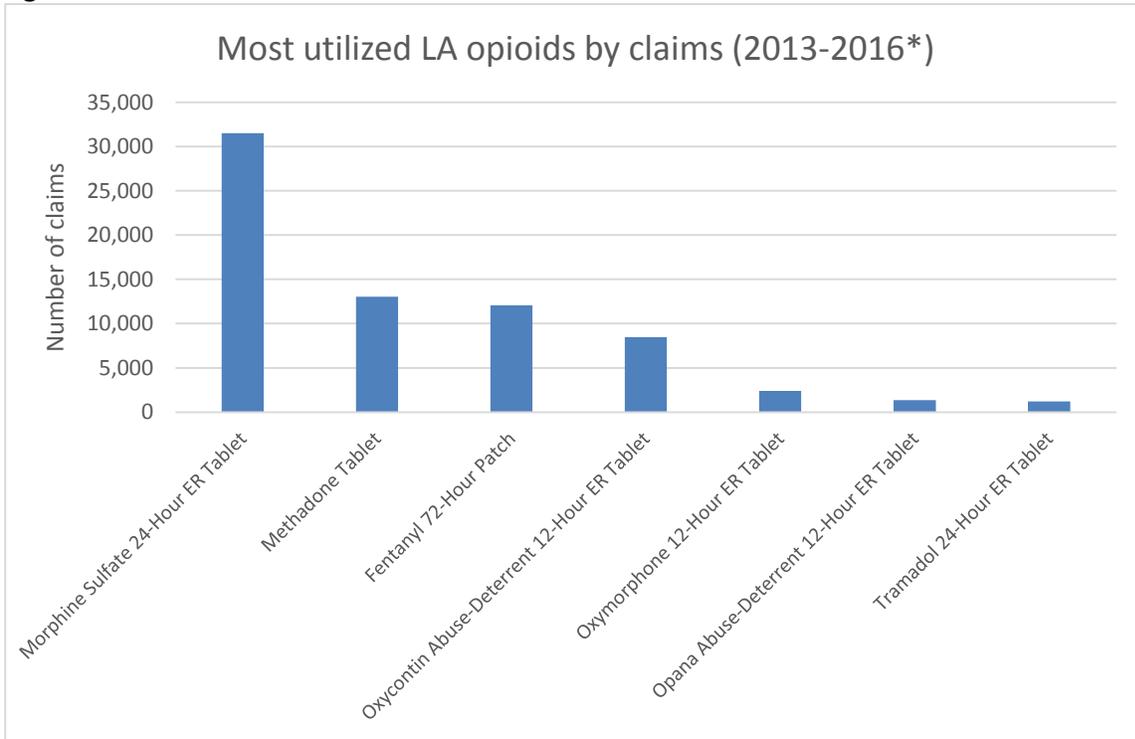
Requests exceeding quantity limits: Most plans require supporting documentation indicating the need for doses higher than the established quantity limits.

- Methadone: Because of its risk of overdose (higher than other pain relievers due to its drug properties) plans (e.g. MassHealth) require a PA for new starters (“defined as anyone who has not filled methadone for 60 out of the last 90 days”) for all doses of methadone.⁷⁷

Utah Medicaid Utilization Data

Overall utilization data for the LA opioids (2013-2016) can be seen in Appendix 2.

(A) 1. Highest utilization



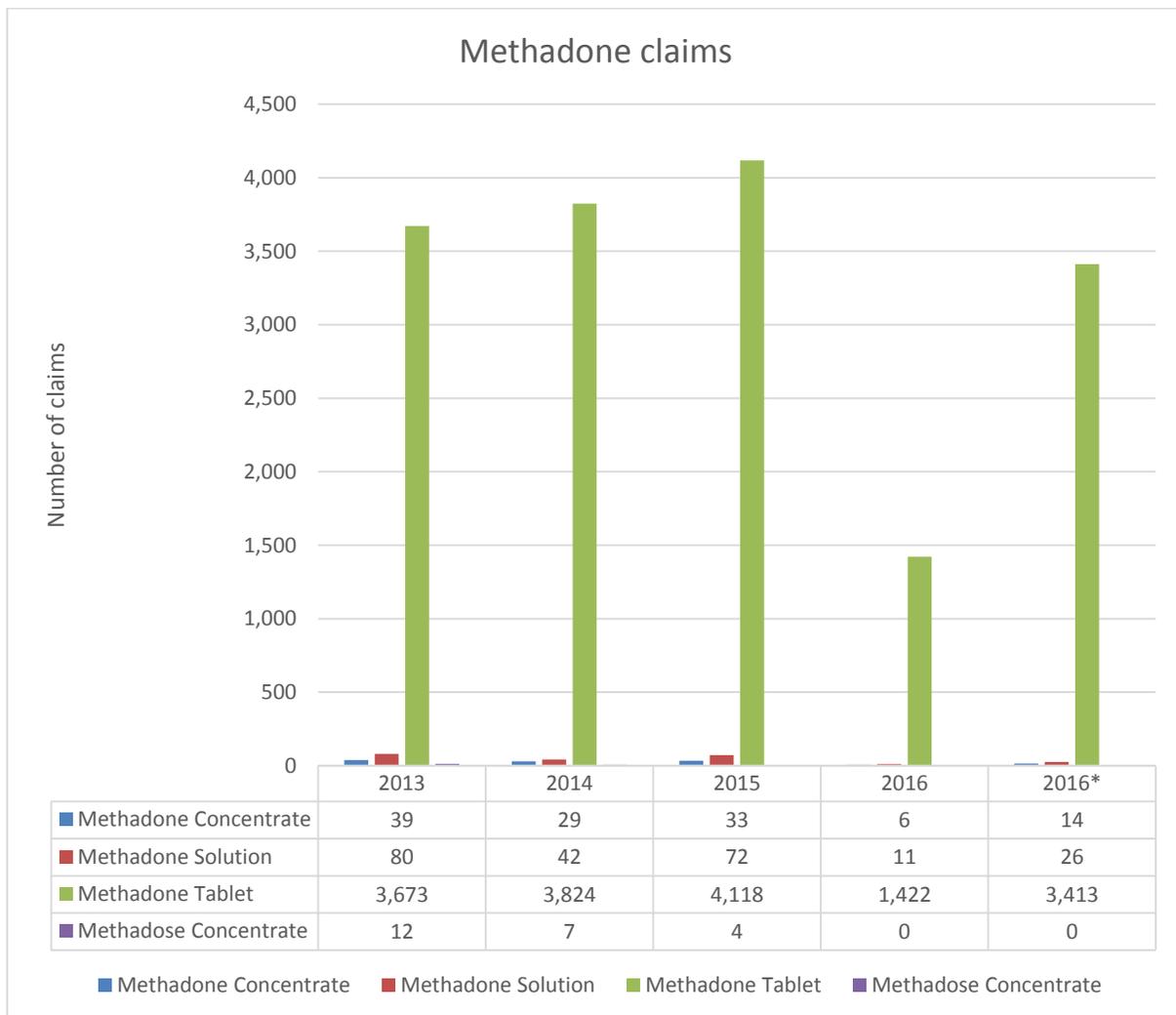
*To date

(A) 2. Overall total utilization of LA opioids

Year	Claims	Patients
2013	19,753	2,908
2014	21,840	3,101
2015	22,145	3,107
2016 to date	9,197	2,192
2016 projected	22,073	-

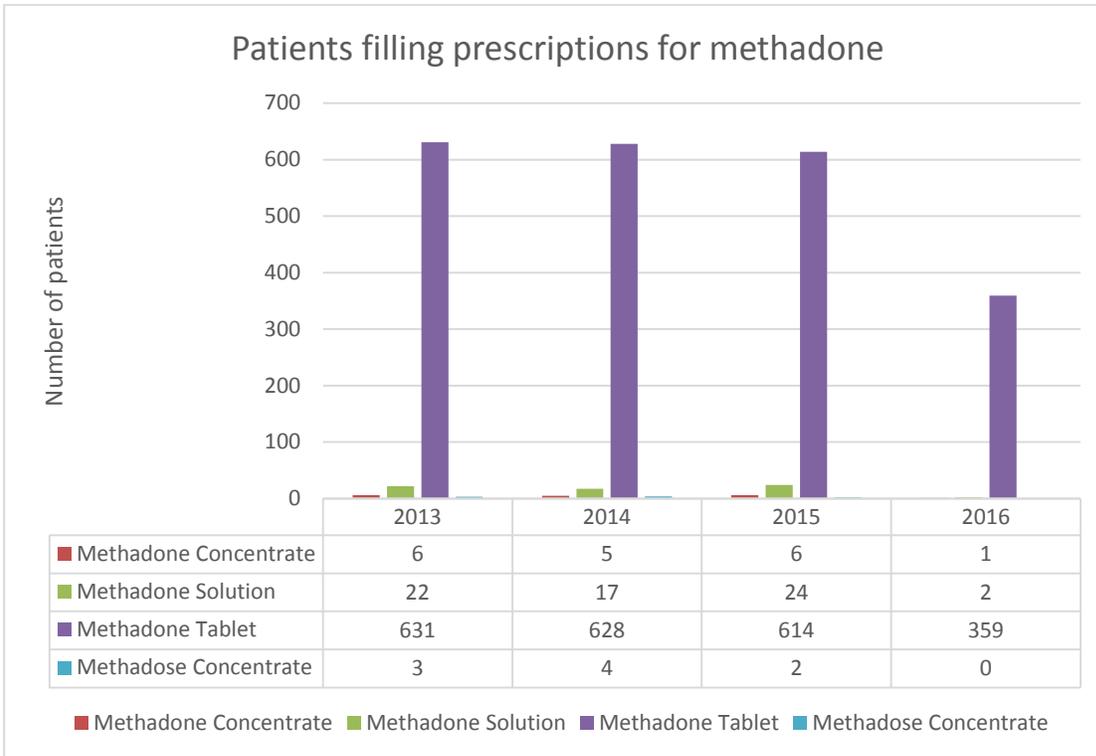
(B) Methadone

The issue of increased use of methadone and its risks, including the disproportionate share of opioid-related overdose deaths associated with methadone prescribed for pain relief purposes, were discussed earlier in the report.⁶⁸ The chart below shows the trend of methadone use in the Utah Medicaid population (by number of claims and by number of patients).

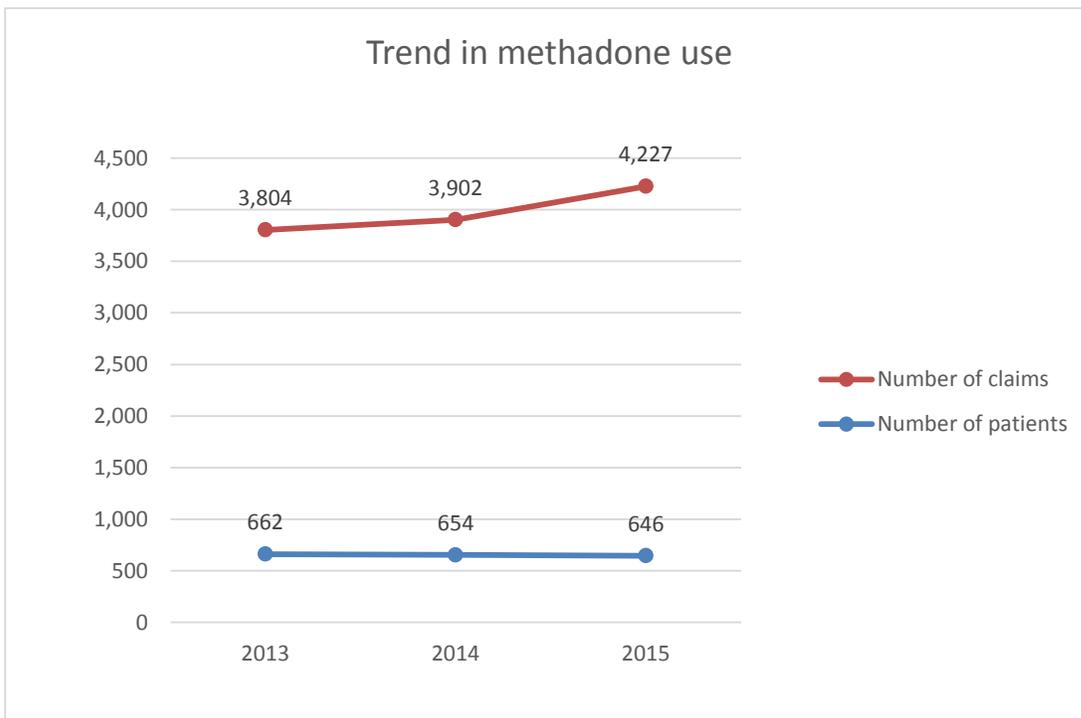


*Projected number of claims (the bar before that shows the actual number of claims to date)

- The number of claims increased by about 200 claims each year between 2013 and 2015. It appears that this has decreased in 2016, but this is an estimated/projected number. It should be kept in mind that methadone is also used in the treatment of opioid abuse treatment.

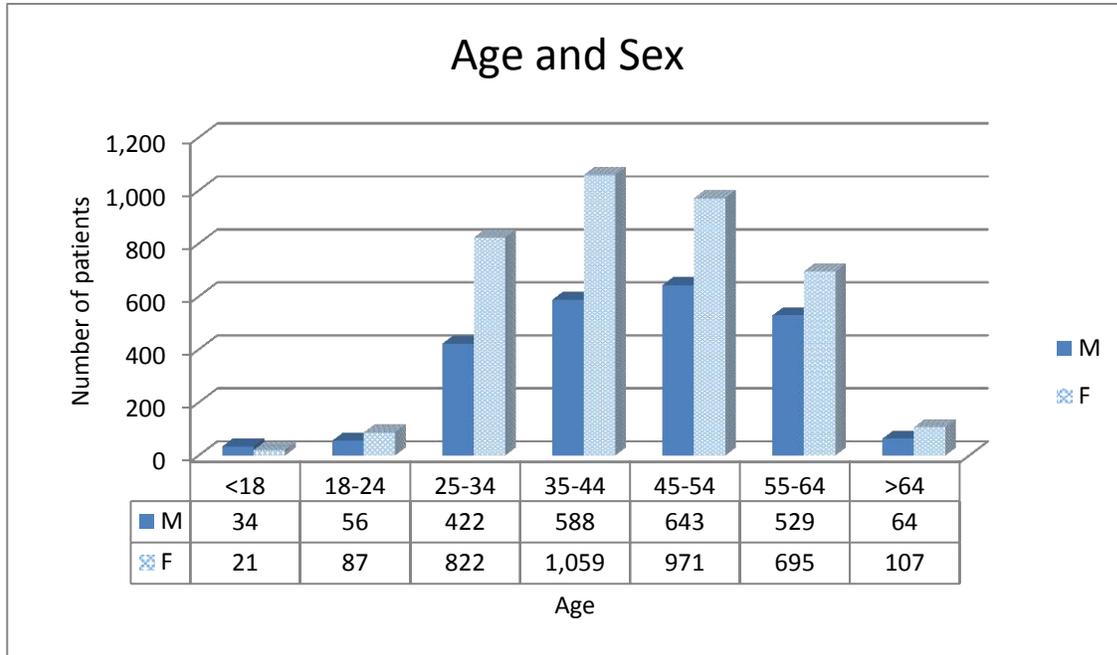


Note that 2016 is only showing number of patients to date.



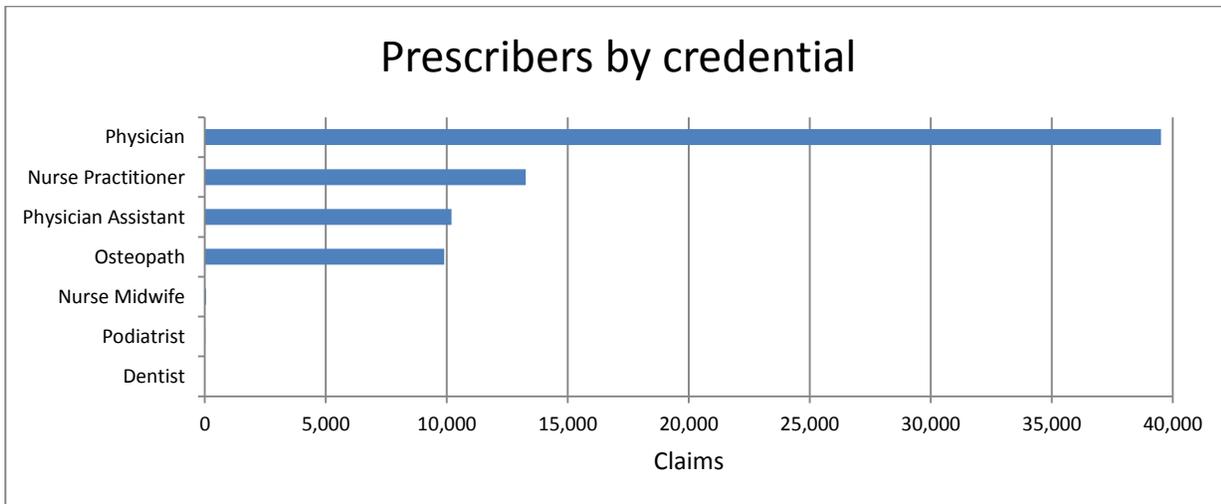
It is reported that methadone use for pain management has been increasing. In the Utah Medicaid population, the number of patients that filled prescriptions for methadone decreased slightly between 2013 and 2015 (keep in mind that this include all patients and not only use for pain). However, the number of claims have increased slightly.

(C) Age and Sex of patients that received LA opioids



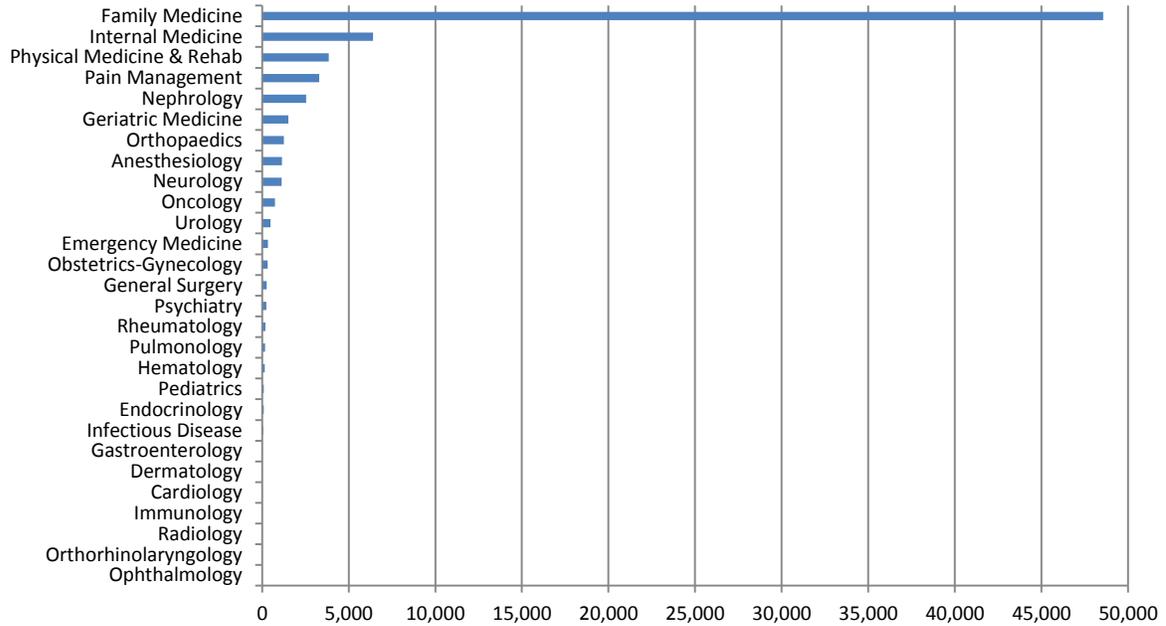
Overall, 55 pediatric patients received LA opioids during this time-frame. In 2016, only 5 pediatric patients have received LA to date; prescribed by physicians, specializing in family medicine. Please refer to appendix 2 for more specific claims information for pediatric patients.

(D) Prescribers of LA opioids



PREScriBER TYPE	TOTAL CLAIMS 2013-16	
Dentist	3	0.00%
Podiatrist	21	0.03%
Nurse Midwife	44	0.06%
Osteopath	9,893	13.56%
Physician Assistant	10,197	13.98%
Nurse Practitioner	13,262	18.18%
Physician	39,515	54.18%
TOTAL CLAIMS	72,935	

Prescribers by specialty



PREScriBER SPECIALTY	TOTAL CLAIMS 2013-16	
Ophthalmology	3	0.00%
Orthorhinolaryngology	4	0.01%
Radiology	5	0.01%
Immunology	6	0.01%
Cardiology	12	0.02%
Dermatology	18	0.02%
Gastroenterology	23	0.03%
Infectious Disease	69	0.09%
Endocrinology	92	0.13%
Pediatrics	99	0.14%
Hematology	150	0.21%
Pulmonology	168	0.23%
Rheumatology	185	0.25%
Psychiatry	244	0.33%
General Surgery	267	0.37%
Obstetrics-Gynecology	315	0.43%
Emergency Medicine	338	0.46%
Urology	490	0.67%
Oncology	748	1.03%
Neurology	1,132	1.55%
Anesthesiology	1,139	1.56%
Orthopaedics	1,254	1.72%
Geriatric Medicine	1,517	2.08%
Nephrology	2,542	3.49%
Pain Management	3,300	4.52%
Physical Medicine & Rehab	3,841	5.27%
Internal Medicine	6,408	8.79%
Family Medicine	48,566	66.59%
TOTAL CLAIMS	72,935	

“The involvement of the anesthesiologist, as a pain specialist, in the management of chronic pain is becoming increasingly evident.”⁸⁰ Prescribers with a specialty in anesthesiology accounted for 1139 claims in the Utah Medicaid population over this time period (1.56% of LA opioid claims).

(E) 1. Potentially inappropriate prescribers of LA opioids

Potentially inappropriate prescribers were identified and additional information is presented in the tables below.

ALL PATIENTS PRESCRIBER TYPE	TOTAL CLAIMS	TOTAL PATIENTS	AVERAGE DURATION OF USE PER RX (DAYS)*	MOST-PRESCRIBED PRODUCT
Dentist	3	3	21	Morphine Sulfate
Nurse Midwife	44	2	28	Fentanyl
Podiatrist	21	3	16	Methadone HCl

PRESCRIBER SPECIALTY	TOTAL CLAIMS	TOTAL PATIENTS	AVERAGE DURATION OF USE PER RX (DAYS)*	MOST-PRESCRIBED PRODUCT
Anesthesiology	1,139	239	27	Morphine Sulfate
Cardiology	12	9	23	Morphine Sulfate
Dermatology	18	3	27	Morphine Sulfate
Emergency Medicine	338	123	23	Morphine Sulfate
Gastroenterology	23	5	28	Fentanyl
Hematology	150	48	29	Morphine Sulfate
Immunology	6	2	19	Morphine Sulfate
Infectious Disease	69	12	28	Morphine Sulfate
Nephrology	2,542	311	28	Morphine Sulfate
Neurology	1,132	191	28	Morphine Sulfate
Obstetrics-Gynecology	315	47	16	Methadone HCl
Ophthalmology	3	3	23	Oxycodone HCl
Orthopaedics	1,254	217	26	Morphine Sulfate
Orthorhinolaryngology	4	4	22	Morphine Sulfate
Pediatrics	99	33	25	Methadone HCl
Psychiatry	244	76	26	Fentanyl
Radiology	5	2	30	Morphine Sulfate
Urology	490	165	27	Morphine Sulfate

*By unique prescription number, taking the difference in days between the first fill of the prescription and the final fill of the prescription and adding the days supplied to the final fill.

(E) 2. Excluding potential patients with cancer/palliative care/sickle cell disease

An attempt was made to exclude patients who potentially have cancer or sickle cell disease (based on diagnosis codes within 6 months; refer to (G) and appendix 2 for definitions) from the potentially inappropriate prescriber table.

Potential patients with cancer, cancer pain, palliative care, or sickle cell disease EXCLUDED

PRESCRIBER TYPE	TOTAL CLAIMS	TOTAL PATIENTS	AVERAGE DURATION OF USE PER RX (DAYS)	MOST-PRESCRIBED PRODUCT
Dentist	1	1	30	Morphine Sulfate
Nurse Midwife	0	0	0	NA
Podiatrist	1	1	10	Oxycodone HCl

PRESCRIBER SPECIALTY	TOTAL CLAIMS	TOTAL PATIENTS	AVERAGE DURATION OF USE PER RX (DAYS)*	MOST-PRESCRIBED PRODUCT
Anesthesiology	342	91	26	Morphine Sulfate
Cardiology	7	5	23	Morphine Sulfate
Dermatology	0	0	0	NA
Emergency Medicine	152	57	24	Morphine Sulfate
Gastroenterology	1	1	14	Methadone HCl
Hematology	2	2	30	Morphine Sulfate
Immunology	6	2	19	Morphine Sulfate
Infectious Disease	14	5	28	Morphine Sulfate
Nephrology	931	147	27	Morphine Sulfate
Neurology	492	100	28	Morphine Sulfate
Obstetrics-Gynecology	202	34	13	Methadone HCl
Ophthalmology	1	1	30	Morphine Sulfate
Orthopaedics	659	122	30	Morphine Sulfate
Orthorhinolaryngology	3	3	25	Methadone HCl
Pediatrics	56	20	23	Methadone HCl
Psychiatry	70	36	21	Fentanyl
Radiology	1	1	30	Morphine Sulfate
Urology	274	91	28	Morphine Sulfate

*By unique prescription number, taking the difference in days between the first fill of the prescription and the final fill of the prescription and adding the days supplied to the final fill.

(F) Outlier prescriber identification

Another way of curbing potential opioid misuse or abuse is to identify the prescribers who are writing a disproportionate number of prescriptions compared to their peers, analyzing these claims, and addressing potential inappropriate prescribing/overprescribing through educational interventions.⁸¹

Top prescribers by claim (All prescribers, no exclusions applied)

PRESCRIBER	TYPE	SPECIALTY	CLAIMS	PATIENTS	PER PATIENT
A	Osteopath	Family Medicine	4444	486	9.14
B	Physician	Family Medicine	3194	951	3.36
C	Nurse Practitioner	Nephrology	2478	308	8.05
D	Physician Assistant	Orthopedics	1033	93	11.11
E	Physician	Family Medicine	852	80	10.65
F	Physician	Geriatric Medicine	830	105	7.90
G	Nurse Practitioner	Family Medicine	819	242	3.38
H	Nurse Practitioner	Family Medicine	728	246	2.96
I	Physician Assistant	Family Medicine	634	138	4.59
J	Nurse Practitioner	Family Medicine	585	64	9.14
K	Physician Assistant	Family Medicine	579	100	5.79
L	Physician Assistant	Physical Medicine & Rehab	564	80	7.05
M	Physician	Geriatric Medicine	545	101	5.40
N	Nurse Practitioner	Family Medicine	538	87	6.18
O	Physician Assistant	Family Medicine	521	55	9.47
P	Nurse Practitioner	Family Medicine	492	67	7.34
Q	Physician	Family Medicine	489	20	24.45
R	Nurse Practitioner	Urology	481	158	3.04
S	Physician	Physical Medicine & Rehab	476	57	8.35
T	Physician	Family Medicine	474	56	8.46
U	Physician	Family Medicine	462	38	12.16
V	Physician Assistant	Family Medicine	460	60	7.67
W	Physician	Physical Medicine & Rehab	460	87	5.29

PRESCRIBER	TYPE	SPECIALTY	CLAIMS	PATIENTS	PER PATIENT
X	Physician Assistant	Family Medicine	455	67	6.79
Y	Physician	Pain Management	436	57	7.65
Z	Nurse Practitioner	Family Medicine	425	61	6.97
AA	Nurse Practitioner	Family Medicine	418	104	4.02
BB	Physician	Family Medicine	418	24	17.42
CC	Physician	Family Medicine	412	36	11.44

Top prescribers by patient average (All prescribers, no exclusions applied)

PRESCRIBER NAME	TYPE	SPECIALTY	CLAIMS	PATIENTS	PER PATIENT
Q	Physician	Family Medicine	489	20	24.45
BB	Physician	Family Medicine	418	24	17.42
U	Physician	Family Medicine	462	38	12.16
CC	Physician	Family Medicine	412	36	11.44
D	Physician Assistant	Orthopedics	1033	93	11.11
E	Physician	Family Medicine	852	80	10.65
O	Physician Assistant	Family Medicine	521	55	9.47
A	Osteopath	Family Medicine	4444	486	9.14
J	Nurse Practitioner	Family Medicine	585	64	9.14
T	Physician	Family Medicine	474	56	8.46
S	Physician	Physical Medicine & Rehab	476	57	8.35
C	Nurse Practitioner	Nephrology	2478	308	8.05
F	Physician	Geriatric Medicine	830	105	7.90
V	Physician Assistant	Family Medicine	460	60	7.67
Y	Physician	Pain Management	436	57	7.65
P	Nurse Practitioner	Family Medicine	492	67	7.34
L	Physician Assistant	Physical Medicine & Rehab	564	80	7.05
Z	Nurse Practitioner	Family Medicine	425	61	6.97
X	Physician Assistant	Family Medicine	455	67	6.79
N	Nurse Practitioner	Family Medicine	538	87	6.18
K	Physician Assistant	Family Medicine	579	100	5.79
M	Physician	Geriatric Medicine	545	101	5.40
W	Physician	Physical Medicine & Rehab	460	87	5.29
I	Physician Assistant	Family Medicine	634	138	4.59
AA	Nurse Practitioner	Family Medicine	418	104	4.02
G	Nurse Practitioner	Family Medicine	819	242	3.38
B	Physician	Family Medicine	3194	951	3.36
R	Nurse Practitioner	Urology	481	158	3.04
H	Nurse Practitioner	Family Medicine	728	246	2.96

(G) Attempt to identify patients with cancer, cancer-related pain, palliative care, or sickle cell disease

DIAGNOSIS	ICD-9	ICD-10	PTS	PERCENT
A) ANY Cancer Encounter - 3 Months	LIST ^a	LIST ^a	2,272	37%
A) ANY Cancer Encounter - 6 Months	LIST ^a	LIST ^a	2,559	42%
A) ANY Cancer Encounter - 2 Years	LIST ^a	LIST ^a	2,971	49%
B) Cancer Related Pain - 3 Months	3383	G893	213	3%
B) Cancer Related Pain - 6 Months	3383	G893	225	4%
B) Cancer Related Pain - 2 Years	3383	G893	235	4%
C) Palliative Care - 3 Months	V667*	Z515*	88	1%
C) Palliative Care - 6 Months	V667*	Z515*	91	1%
C) Palliative Care - 2 Years	V667*	Z515*	92	2%
D) Sickle Cell Disease - 3 Months	2826*	D57*	5	0%
D) Sickle Cell Disease - 6 Months	2826*	D57*	6	0%
D) Sickle Cell Disease - 2 Years	2826*	D57*	7	0%
B, C OR D - 3 Months			284	5%
B, C OR D - 6 Months			299	5%
B, C OR D - 2 Years			311	5%
A, B, C OR D - 3 Months			2,272	37%
A, B, C OR D - 6 Months			2,559	42%
A, B, C OR D - 2 Years			2,971	49%

TOTAL PATIENTS USING A LONG ACTING OPIOID 6,098

^a List of diagnoses and diagnosis codes potentially indicating cancer adapted from http://seer.cancer.gov/tools/conversion/2014/ICD9CM_to_ICD10CM_2014CF.pdf.

This adapted list is a 63-page document and therefore not included as an appendix, but available on request.

A detailed summary of the utilization table by product with these diagnoses can be seen in appendix 2. The highlighted group/definition (A, B, C, or D diagnoses within 6 months) was used to exclude potential patients with cancer or sickle cell disease in some sections of the report e.g. (E) 2.

(H) Units dispensed

The number of units categorized into specific categories (≤ 30 ; >30 to ≤ 60 ; >60 to ≤ 90 ; >90 and for transdermal: ≤ 11 ; 12 to ≤ 15 ; >15) can be seen in appendix 2 (first shown as all claims, and followed by an attempt to exclude patients with cancer/sickle cell disease).

(I) Proposed quantity limits

The number of claims and patients falling outside the proposed quantity limits are shown in appendix 2 (first shown as all claims, and followed by an attempt to exclude patients with cancer/sickle cell disease).

Conclusions

Well-controlled clinical studies on opioid-prescribing methods for chronic pain are lacking, and evidence of long-term efficacy of opioids for chronic non-cancer pain is limited.^{13,38} Long-term opioid use is controversial, but may be the only available option for some patients after other treatment options have been exhausted and careful consideration of associated benefits and risks. The CDC guidelines which have been endorsed by the FDA re-iterate “well-accepted medical principles of drug prescribing: to use the lowest effective dose for the shortest possible duration.”¹⁰ Opioid use is associated with serious risks (including misuse, abuse and overdose), and excessive prescriptions and fills lead to leftover medications which is an important source of opioids that are misused or diverted.^{19,20} There is insufficient evidence to support the use of LA over SA opioids, but it is a well-accepted standard current practice and believed to provide better control of pain around the clock, and convenient once- (24-hourly) or twice-daily (12-hourly) administration.

The Utah Medicaid Utilization Data indicates potentially inappropriate prescribing and use of LA opioids in the Utah Medicaid populations which can result in opioid use disorder, drug-related deaths, costly medical complications (i.e. nonfatal overdoses, falls and fractures, drug-drug related interactions, neonatal conditions, emergency visits, hospital care), indirect costs (i.e. criminal justice costs and costs associated with lost productivity) and an “incalculable amount of emotional suffering.”⁶⁸ Strategies as suggested by the CMS (education, encouraging use of safer alternatives particularly to methadone, reassessing PDL placement, introducing clinical criteria, prior authorization, step therapy, quantity limits, and DUR processes and activities) therefore should be “revisited continually as the nature of the opioid epidemic evolves and new information emerges”.

“Decreasing opioid misuse and abuse, while at the same time assuring that patients with chronic and acute pain have access to treatment to control their pain, needs to be a major goal for all health professionals, government, pharmaceutical manufacturers, and payers and will require a substantial effort from all parties.”⁷

Appendix 1 – Drug information

Table 5: Extended-release/long-acting opioid products (opiate agonists) & opioid-naïve patients warnings – Adapted from Micromedex, Lexicomp, product labels and Narcotic summary table^{9,21,22,82}

Dosage form & How supplied	Brand name	Indication	Opioid-naïve patients	Notes
Fentanyl				
<p>Fentanyl transdermal patches</p> <p>Generic Transdermal Patch, Extended Release: 12 MCG/1 HR, 25 MCG/1 HR, 37.5 MCG/1 HR, 50 MCG/1 HR, 62.5 MCG/1 HR, 75 MCG/1 HR, 87.5 MCG/1 HR, 100 MCG/1 HR</p> <p>Duragesic Transdermal Patch, Extended Release: 12 MCG/1 HR, 25 MCG/1 HR, 50 MCG/1 HR, 75 MCG/1 HR, 100 MCG/1 HR</p>	<p>Duragesic Generic</p>	<p>ONLY for use in the management of chronic, moderate to severe pain requiring around-the-clock opioid therapy not managed by other means in patients who have demonstrated opioid tolerance and require a total daily dose equivalent to the fentanyl 25 mcg/hr transdermal patch.</p>	<p>Management of acute or postoperative pain in opiate-naïve patients is contraindicated.</p> <p>Substantial interpatient variability exists in relative potency. Therefore, it is safer to underestimate a patient’s daily fentanyl requirement and provide breakthrough pain relief with rescue medication (eg, immediate release opioid) than to overestimate requirements.</p> <p>Initial dose recommendations based on daily oral morphine requirement: initiate at 25 mcg/hr for oral morphine doses of 60 to 134 mg/day; initiate at 50 mcg/hr for oral morphine doses of 135 to 224 mg/day; initiate at 75 mcg/hr for oral morphine doses of 225 to 314 mg/day; initiate at 100 mcg/hr for oral morphine doses of 315 to 404 mg/day; initiate at 125 mcg/hr for oral morphine doses of 405 to 494 mg/day; initiate at 150 mcg/hr for oral morphine doses of 495 to 584 mg/day; initiate at 175 mcg/hr for oral morphine doses of 585 to 674 mg/day; initiate at 200 mcg/hr for oral morphine doses of 675 to 764 mg/day; initiate at 225 mcg/hr for oral morphine doses of 765 to 854 mg/day; initiate at 250 mcg/hr for oral morphine doses of 855 to 944 mg/day; initiate at 275 mcg/hr for oral morphine doses of 945 to 1034 mg/day; initiate at 300 mcg/hr for oral morphine doses of 1035 to 1124 mg/day; apply TRANSDERMALLY; replace patch every 72 hours; for delivery rates exceeding 100 mcg/hr multiple patches may be used</p>	<p>Titrate slowly. Analgesia reaches peak 12 hrs after application; may persist 12-24 hrs after removal. High equianalgesic potency.</p> <p>Discontinue or taper all other around-the-clock or extended release opioids when initiating therapy with fentanyl transdermal patch.</p> <p><u>Dose titration:</u> do not increase dose in first 3 days; first dose titration should be based on the daily dose of supplemental opioid analgesics required on day 2 or 3; subsequent titrations should occur no more often than every 6 days and dose increases should be based on daily supplemental opioid dose using the ratio 45 mg/24 hours of oral morphine to a 12 mcg/hr increase in transdermal fentanyl ; <u>a small number of patients may require patch application every 48 hours</u>; a dose increase should be evaluated before considering a change in dosing interval</p> <p>Fatal overdose have occurred when pets, children and adults were accidentally exposed to the fentanyl patch.</p>

Dosage form & How supplied	Brand name	Indication	Opioid-naïve patients	Notes
Hydromorphone				
Hydromorphone Oral Tablet ER 24 Hour Abuse-Deterrent 8 MG 12 MG 16 MG 32 MG	Exalgo Generic	For use in opioid-tolerant patients only with moderate to severe chronic pain. It is for continuous analgesia only and is not intended for use on an as needed basis (ie, PRN). It should be swallowed whole; not broken, chewed, opened, dissolved, or crushed.	Not to be used in opioid-naïve patients. <i>Opioid-tolerant patients:</i> Discontinue or taper all other extended-release opioids when starting therapy. <i>Individualization of dose:</i> Suggested recommendations for converting to Exalgo from other analgesics are presented in Lexicomp, but when selecting the initial dose, other characteristics (eg, patient status, degree of opioid tolerance, concurrent medications, type of pain, risk factors for addiction, abuse, and misuse) should also be considered. Pain relief and adverse events should be assessed frequently.	Patients taking opioids chronically may become tolerant and require doses higher than the usual dosage range to maintain the desired effect. Tolerance can be managed by appropriate dose titration. There is no optimal or maximal dose for hydromorphone in chronic pain. The appropriate dose is one that relieves pain throughout its dosing interval without causing unmanageable side effects. <u>Potent opioid:</u> even one dose of hydromorphone ER can result in fatal overdose (especially in children)
Morphine				
Morphine Extended-release Generic Oral Capsule, Extended Release: 10 MG, 20 MG, 30 MG, 50 MG, 60 MG, 80 MG, 100 MG Oral Capsule, Extended Release, 24 HR: 30 MG, 45 MG, 60 MG, 75 MG, 90 MG, 120 MG Oral Tablet, Extended Release: 15 MG, 30 MG, 60 MG, 100 MG, 200 MG MS Contin Oral Tablet, Extended Release: 15 MG, 30 MG, 60 MG, 100 MG, 200 MG Kadian Oral Capsule, Extended Release: 10 MG, 20 MG, 30 MG, 40 MG, 50 MG, 60 MG, 80 MG, 100 MG, 200 MG Avinza Not in Micromedex & Lexicomp & FDA information state Discontinued	Morphine ER Tablets (GENERIC, MS CONTIN, ORAMORPH) Morphine ER Capsules 24 hour (KADIAN, AVINZA, Generic)	<u>Avinza(R):</u> in opioid-naïve patients, a starting dose of 30 mg ORALLY every 24 hours , with dosage adjustments of not greater than 30 mg every 4 days, <u>MAX 1600 mg/day due to fumaric acid content</u> ; conversion to Avinza(TM), administer patient's total daily morphine requirement <u>once a day</u> ; only opioid-tolerant patients should use 45, 60, 75, 90, and 120 mg capsules. <u>Kadian(R):</u> initial conversion to Kadian(R), total daily morphine requirement ORALLY once <u>every 24 hours</u> or one-half of the estimated total daily requirement once <u>every 12 hours</u> ; in patients with no proven opioid tolerance, start only on the 10 mg or 20 mg strength , and dosage may be adjusted at a 20-mg increment no more frequently than every-other-day; 100 mg and 200 mg capsules are for use only in opioid-tolerant patients. <u>MS Contin(R):</u> initial conversion to MS Contin(R) one-half of the estimated total daily morphine requirement ORALLY once <u>every 12 hours</u> , or at one-third of the total daily morphine requirement <u>every 8 hours</u> ; the 100- and 200-mg tablets are intended for use in opioid-tolerant patients requiring daily morphine equivalent dosages of 200 mg or more for the 100-mg tablet and 400 mg or more for the 200-mg tablet. <u>Oramorph(R) SR:</u> one-third of the patient's daily morphine requirement ORALLY every 8 hours or one-half of the daily morphine dosage requirement every 12 hours; the 30-mg tablet strength is recommended for the initial titration period, particularly among patients whose daily morphine requirements are less than or equal to 120 mg/day. <u>Extended-release tablets</u> (Mallinckrodt, Inc) one-half of the estimated total daily requirement ORALLY once <u>every 12 hours</u> , or at one-third of the total daily requirement <u>every 8 hours</u> ; when the daily morphine requirement is expected to be less than 60 mg per day, then the 15-mg tablet strength is recommended and when the daily requirement is expected to be between 60 mg to 120 mg per day, then the 30-mg tablet strength is recommended.	There are once-daily and sprinkle versions, but they are branded, more expensive. Caution in severe renal failure; accumulation of metabolites can cause agitation, delirium. Can try once-daily dosing, though still may need twice daily. Unlike regular morphine, there are brand-specific maximal doses. May open cap & sprinkle, but do not crush/chew/dissolve. Combination of immediate & delayed-release. Very expensive. Caution in severe renal failure; accumulation of metabolites can cause agitation, delirium. Accidental ingestion of even one dose can result in fatal overdose (especially in children).	

Dosage form & How supplied	Brand name	Indication	Opioid-naïve patients	Notes
Oxycodone				
<p>Oxycodone Extended-release tablet</p> <p>Generic Oral Tablet, Extended Release: 10 MG, 15 MG, 20 MG, 30 MG, 40 MG, 60 MG, 80 MG</p> <p>OxyCONTIN Oral Tablet, Extended Release: 10 MG, 15 MG, 20 MG, 30 MG, 40 MG, 60 MG, 80 MG</p>	Oxycontin Generic	For continuous, around the clock analgesia for an extended period of time; not for use on an as needed basis.	<p>Black Box warning: The 60 mg and 80 mg tablets, a single dose greater than 40 mg, or a total daily dose greater than 80 mg, are only for use in opioid-tolerant patients as they may cause fatal respiratory depression when administered to patients who are not tolerant to the respiratory depressant effects of opioids.</p> <p>Opioid-naïve: 10 mg every 12 hours.</p>	<p>Note: Some clinicians have reported that <u>in certain chronic pain patients, more frequent dosing (ie, every 8 hours) is required for effective pain relief</u> (Gallagher 2007; Marcus 2004; Nicholson 2006), <u>although dosing more frequently than every 12 hours is not recommended by the manufacturer, and safety and efficacy has not been established.</u></p> <p>Accidental ingestion of even one dose can result in fatal overdose (especially in children).</p>
<p>Extended-release capsules: 9 mg (equivalent to 10 mg oxycodone HCl) 13.5 mg (equivalent to 15 mg oxycodone HCl) 18 mg (equivalent to 20 mg oxycodone HCl) 27 mg (equivalent to 30 mg oxycodone HCl) 36 mg (equivalent to 40 mg oxycodone HCl).</p>	Xtampza ER	For the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate (e.g., nonopioid analgesics or immediate-release opioids are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain)	For opioid-naïve and opioid non-tolerant patients, initiate with 9 mg (equivalent to 10 mg oxycodone HCl) capsules orally every 12 hours with food.	The daily dose of XTAMPZA ER must be limited to a maximum of 288 mg per day which is eight 36 mg capsules (equivalent to 320 mg oxycodone HCl per day). The safety of the excipients in XTAMPZA ER for doses over 288 mg/day has not been established.
<p>Oral extended-release capsules: Oxycodone hydrochloride 7.5 mg and acetaminophen 325 mg</p>	Xartemis XR	<p>Management of acute pain severe enough to require opioid treatment and for which alternative treatment options are inadequate.</p> <p>Limitations of use: Because of the risks of addiction, abuse, misuse, overdose, and death with opioids, even at recommended doses, reserve extended-release (ER) for use in patients for whom alternative treatment options (eg, nonopioid analgesics) are ineffective.</p>	Usual dose: 2 tablets every 12 hours; the second initial dose may be administered as early as 8 hours after the first initial dose if needed; subsequent doses are to be administered <u>2 tablets every 12 hours. Do not exceed acetaminophen 4 g daily.</u>	<p>Note: Initial dose is based on the oxycodone content; however, the maximum daily dose is based on the acetaminophen content.</p> <p>NOTE: Oxycodone/acetaminophen ER is not interchangeable with other oxycodone/acetaminophen products because of differing pharmacokinetic profiles that affect the frequency of administration.</p> <p>Due to the potential for acetaminophen hepatotoxicity at doses higher than 4000 mg/day, XARTEMIS XR should not be used</p>

Dosage form & How supplied	Brand name	Indication	Opioid-naïve patients	Notes
		not tolerated, or would be otherwise inadequate.		with other acetaminophen-containing products.
Oxymorphone				
Oxymorphone Tablet ER 12 Hour Generic & Opana ER Oral Tablet, Extended Release: 5 MG, 7.5 MG, 10 MG, 15 MG, 20 MG, 30 MG, 40 MG	Opana ER (Abuse-deterrent) Generic	Management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate. NOT intended for use as an as needed analgesic. Limitations of use: Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with ER opioid formulations, reserve oxymorphone ER for use in patients for whom alternative treatment options (eg, nonopioid analgesics, immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient pain management. Not indicated as an as-needed analgesic.	Opioid-Naïve Patients: Initiate treatment with 5 mg every 12 hours.	Expensive. Give PO doses 1 hr before or 2 hours after meals. High equianalgesic potency. Accidental ingestion of even one dose can result in fatal overdose (especially in children).
Hydrocodone				
Hydrocodone ER capsules 12 hour Capsule ER Abuse-Deterrent Zohydro ER Oral Capsule, Extended Release: 10 MG, 15 MG, 20 MG, 30 MG, 40 MG, 50 MG Tablet ER 24 hour Abuse-	Zohydro ER Hysingla ER	Management of pain severe enough to require daily around-the-clock opioid, long-term treatment and for which alternative treatment options (eg, nonopioid analgesics or immediate release opioids) are inadequate	Note: Single oral doses >40 mg, a total daily dose ≥80 mg, the 50 mg extended-release capsules (Zohydro ER), and Hysingla(TM) ER total daily doses of 80 mg/day or higher are only for patients who are opioid tolerant. Hysingla ER: Initial: 20 mg once daily. Dose increases may occur in increments of 10 to 20 mg every 3 to 5 days as needed to achieve adequate analgesia Zohydro ER: Initial: 10 mg every 12 hours. Dose increases	Black box warning regarding addiction potential, respiratory depression, accidental exposure (Accidental consumption of even 1 dose of hydrocodone ER, especially by children, can result in a fatal overdose), neonatal opioid withdrawal syndrome, interaction with alcohol, and CYP450 3A4 interaction (concomitant use of

Dosage form & How supplied	Brand name	Indication	Opioid-naïve patients	Notes
Deterrent Hysingla ER Oral Tablet, Extended Release: 20 MG, 30 MG, 40 MG, 60 MG, 80 MG, 100 MG, 120 MG			may occur in increments of 10 mg every 12 hours every 3 to 7 days as needed to achieve adequate analgesia	hydrocodone ER with all CYP450 3A4 inhibitors may result in an increase in hydrocodone plasma concentrations, which could increase or prolong adverse drug effects and may cause potentially fatal respiratory depression).
Tapentadol				
Tapentadol Tablets Extended Release 12 Hour Nucynta ER Oral Tablet, Extended Release: 50 MG, 100 MG, 150 MG, 200 MG, 250 MG	Nucynta ER	<p>Pain or neuropathic pain associated with diabetic peripheral neuropathy (DPN) severe enough to require daily, around-the-clock, long-term opioid analgesia and for which alternative treatments are inadequate.</p> <p>Limitations of use: Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with extended-release opioid formulations, reserve tapentadol ER for use in patients for whom alternative treatment options (eg, nonopioid analgesics, immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain. Tapentadol ER is not indicated as an as-needed analgesic.</p>	Opioid naïve: Initial: 50 mg twice daily (recommended interval: ~12 hours); titrate in increments of 50 mg no more frequently than twice daily every 3 days to effective dose (<u>therapeutic range: 100-250 mg twice daily</u>) (<u>maximum dose: 500 mg/day</u>)	<p>Extended release tablets: [U.S. Boxed warning]: NOT intended for use as an as-needed analgesic; NOT intended for the management of acute or postoperative pain; approved for the treatment of chronic pain only (not an as-needed basis).</p> <p>Extended release tablets: [U.S. Boxed Warning]: Extended release tablets must be swallowed whole and should NOT be split, crushed, broken, chewed, or dissolved.</p> <p>Accidental ingestion of even one dose can result in fatal overdose (especially in children).</p>

Dosage form & How supplied	Brand name	Indication	Opioid-naïve patients	Notes
Tramadol				
<p>Tramadol Oral tablet ER 24 Hour</p> <p>Oral ER Capsule 24 Hour</p> <p>Generic Oral Capsule, Extended Release: 100 MG, 150 MG, 200 MG Oral Tablet, Extended Release: 100 MG, 200 MG, 300 MG</p> <p>ConZip Oral Capsule, Extended Release: 100 MG, 200 MG, 300 MG</p> <p>Ultram ER Oral Tablet, Extended Release: 100 MG, 200 MG, 300 MG</p>	<p>Ultram ER Generic</p> <p>ConZip (ConZip extended release capsules are formulated as a biphasic product, providing immediate and extended release components) Generic</p>	<p>For patients requiring around-the-clock management of moderate to moderately-severe pain for an extended period of time</p>	<p>Patients not currently on immediate-release tramadol: 100 mg <u>once daily</u>; titrate every 5 days (ConZip™, Ultram® ER); <u>maximum dose: 300 mg daily</u></p> <p>Extended release tablets: Caution patients to swallow tablets whole. Rapid release absorption of tramadol from tablets that are broken, crushed, or chewed may lead to a potentially-lethal overdose.</p>	<p>Low potency, so probably not a practical maintenance choice in most chronic pain settings.</p> <p><u>Off-label use:</u> Use of tramadol for the treatment of <u>restless legs syndrome (RLS)</u> is limited to data from a noncontrolled trial that demonstrated subjective improvement in the majority of patients. American Academy of Sleep Medicine guidelines recognize very low evidence for opioids in general. European Federation of Neurological Societies/European Neurological Society/European Sleep Research Society joint task force guidelines on management of RLS consider data insufficient to make a recommendation regarding opioids. These guidelines also note that a case report of tramadol use in RLS describes the first case of augmentation in this drug class.</p>
Methadone				
<p>Methadone Injection Oral concentrate, solution Tablets</p> <p>Generic Injection Solution: 10 MG/1 ML Intravenous Solution: 10 MG/1 ML Oral Solution: 5 MG/5 ML, 10 MG/5 ML, 10 MG/1 ML Oral Tablet: 5 MG, 10 MG Oral Tablet for Suspension: 40 MG</p> <p>Diskets Dispersible Oral Tablet: 40 MG</p>	<p>Dolophine tablets Methadone Intensol (solution) Methadose (dispersible tablets or solution)</p>	<p>Pain (Moderate to Severe): Opioid naïve patients: (initial) 2.5 mg ORAL/IV/IM/SubQ every 8 hr (guideline dosing)⁸³</p> <p>Pharmacokinetic properties and high interpatient variability in absorption, metabolism, and relative analgesic potency of methadone necessitates a cautious and individualized approach to prescribing; careful dose initiation and titration necessary</p>	<p>Manufacturer’s labeling: Opioid-naïve: Initial oral dose: 2.5 mg every 8 to 12 hours IV: Initial: 2.5 to 10 mg every 8 to 12 hours; titrate slowly to effect; may also be administered by SubQ or IM injection (manufacturer’s labeling)</p> <p>Alternative recommendations: Opioid-naïve: Oral: <i>Gradual titration (for chronic noncancer pain and situations where frequent monitoring is unnecessary):</i> Initial: 2.5 mg every 8 hours; may increase dose by 2.5 mg per dose (Va/DoD, 2010) or 5 mg per day (Chou, 2014) every 5 to 7 days. Once a stable dose is reached, the dosing interval may be extended to every 8 to 12 hours, or longer (Va/DOD, 2010).</p>	<p>Very long, variable half-life. Titrate very slowly to effect; it may take 3-5 days to achieve full analgesic effect. Peak sedation and respiratory depressant effects may occur later than peak pain effect; always write “hold for sedation.” Use a very conservative interpretation of equianalgesic tables. Relatively safe with renal disease.</p> <p>Limitations of use: Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with long-acting opioids, reserve methadone for use in patients for whom alternative analgesic</p>

Dosage form & How supplied	Brand name	Indication	Opioid-naïve patients	Notes
<p>Dolophine HCl Oral Tablet: 5 MG, 10 MG</p> <p>Methadone HCl Intensol Oral Solution: 10 MG/1 ML</p> <p>Methadose Oral Solution: 10 MG/1 ML Oral Tablet: 40 MG Oral Tablet for Suspension: 40 MG</p>		<p>Detoxification: Detoxification and maintenance treatment of opioid addiction (heroin or other morphine-like drugs), in conjunction with appropriate social and medical services.</p>		<p>treatment options (eg, nonopioid analgesics, immediate-release opioid analgesics) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain. Methadone is not for use as an as-needed analgesic.</p>

Appendix 2 – Utah Medicaid Utilization Data

LONG ACTING OPIOIDS - ALL CLAIMS

GENERIC	DESCRIPTION	2013		2014		2015		ACTUAL	PROJECTED	2016*	ALL	
		CLAIMS	PATIENTS	CLAIMS	PATIENTS	CLAIMS	PATIENTS	CLAIMS	CLAIMS	PATIENTS	CLAIMS	PATIENTS
Fentanyl	Duragesic 72-Hour Patch	10	2	21	1	24	1	15	36	1	70	2
Fentanyl	Fentanyl 72-Hour Patch	3,297	586	3,806	627	3,465	631	1,490	3,576	394	12,048	1,480
Fentanyl HCl	Ionsys Patch	0	0	0	0	0	0	0	0	0	0	0
Hydrocodone Bitartrate	Hysingla Abuse-Deterrent 24-Hour Extended Release Tablet	0	0	0	0	21	5	19	46	4	40	6
Hydrocodone Bitartrate	Zohydro 12-Hour Extended Release Capsule	0	0	3	1	14	4	3	7	3	20	6
Hydrocodone Bitartrate	Zohydro Abuse-Deterrent 12-Hour Extended Release Capsule	0	0	0	0	12	4	13	31	4	25	6
Hydromorphone HCl	Exalgo Abuse-Deterrent 24-Hour Extended Release Tablet	63	15	46	10	0	0	0	0	0	109	17
Hydromorphone HCl	Hydromorphone Abuse-Deterrent 24-Hour Extended Release Tablet	0	0	15	3	33	4	4	10	1	52	6
Methadone HCl	Methadone Concentrate	39	6	29	5	33	6	6	14	1	107	10
Methadone HCl	Methadone Solution	80	22	42	17	72	24	11	26	2	98	52
Methadone HCl	Methadone Tablet	3,673	631	3,824	628	4,118	614	1,422	3,413	359	13,026	1,248
Methadone HCl	Methadose Concentrate	12	3	7	4	4	2	0	0	0	23	9
Morphine Sulfate	Duramorph Injectable Solution	0	0	0	0	0	0	0	0	0	0	0
Morphine Sulfate	Infumorph Injectable Solution	0	0	0	0	0	0	0	0	0	0	0
Morphine Sulfate	Kadian 24-Hour Extended Release Capsule	44	9	104	24	120	24	52	125	12	320	50
Morphine Sulfate	Morphine Sulfate 24-Hour Extended Release Capsule	306	77	167	46	48	14	30	72	8	551	112
Morphine Sulfate	Morphine Sulfate 24-Hour Extended Release Tablet	8,071	1,365	9,617	1,610	9,800	1,626	4,136	9,926	1,083	31,532	3,454

LONG ACTING OPIOIDS - ALL CLAIMS

GENERIC	DESCRIPTION	2013		2014		2015		ACTUAL	PROJECTED	2016*	ALL	
		CLAIMS	PATIENTS	CLAIMS	PATIENTS	CLAIMS	PATIENTS	CLAIMS	CLAIMS	PATIENTS	CLAIMS	PATIENTS
Morphine Sulfate	MS Contin 24-Hour Extended Release Tablet	0	0	0	0	2	2	0	0	0	2	2
Morphine Sulfate Beads	Avinza 24-Hour Extended Release Capsule	67	8	32	5	0	0	0	0	0	99	8
Morphine Sulfate Beads	Morphine Sulfate 24-Hour Extended Release Capsule	0	0	16	2	19	4	11	26	3	46	6
Morphine Sulfate Liposome	Depodur Injectable Suspension	0	0	0	0	0	0	0	0	0	0	0
Oxycodone HCl	Oxycodone Abuse-Deterrent 12-Hour Extended Release Tablet	0	0	11	6	166	43	155	372	52	331	80
Oxycodone HCl	Oxycontin Abuse-Deterrent 12-Hour Extended Release Tablet	2,806	370	2,478	346	2,314	323	878	2,107	218	8,471	704
Oxycodone-Acetaminophen	Xartemis 12-Hour Extended Release Tablet	0	0	1	1	0	0	0	0	0	1	1
Oxymorphone HCl	Opana 12-Hour Extended Release Tablet	17	13	5	5	0	0	0	0	0	22	18
Oxymorphone HCl	Opana Abuse-Deterrent 12-Hour Extended Release Tablet	318	109	377	118	437	104	230	552	75	1,362	315
Oxymorphone HCl	Oxymorphone 12-Hour Extended Release Tablet	265	59	682	106	928	160	506	1,214	146	2,381	298
Tapentadol HCl	Nucynta 12-Hour Extended Release Tablet	163	40	99	27	117	28	72	173	22	451	88
Tramadol HCl	Ryzolt 24-Hour Extended Release Tablet	2	2	0	0	0	0	0	0	0	2	2
Tramadol HCl	Tramadol 24-Hour Extended Release Tablet	414	103	349	83	295	64	144	346	45	1,201	209
Tramadol HCl	Ultram 24-Hour Extended Release Tablet	106	25	109	30	103	36	0	0	0	318	73
TOTALS		19,753	2,908	21,840	3,101	22,145	3,107	9,197	22,073	2,192	72,935	6,098

LONG ACTING OPIOIDS - PEDIATRIC CLAIMS (Only products with utilization are shown)

GENERIC	DESCRIPTION	2013		2014		2015		ACTUAL	PROJECTED	2016*	ALL	
		CLAIMS	PATIENTS	CLAIMS	PATIENTS	CLAIMS	PATIENTS	CLAIMS	CLAIMS	PATIENTS	CLAIMS	PATIENTS
Fentanyl	Fentanyl 72-Hour Patch	10	2	0	0	0	0	0	0	0	10	2
Methadone HCl	Methadone Solution	33	11	20	11	53	19	1	2	1	107	34
Methadone HCl	Methadone Tablet	4	1	5	3	2	2	0	0	0	11	5
Morphine Sulfate	Morphine Sulfate 24-Hour Extended Release Tablet	19	4	14	3	48	7	11	26	3	92	12
Oxycodone HCl	Oxycodone Abuse-Deterrent 12-Hour Extended Release Tablet	0	0	0	0	0	0	1	2	1	1	1
Oxycodone HCl	Oxycontin Abuse-Deterrent 12-Hour Extended Release Tablet	4	1	1	1	0	0	0	0	0	5	2
Tramadol HCl	Tramadol 24-Hour Extended Release Tablet	0	0	1	1	0	0	0	0	0	1	1
TOTALS		70	18	41	18	103	28	13	31	5	227	55

CANCER AND SICKLE DIAGNOSES - ALL LONG ACTING OPIOID CLAIMS

GENERIC	DESCRIPTION	A) Cancer History			B) Cancer Pain			C) Palliative Care			D) Sickle Cell Disease			B, C or D			A, B, C or D		
		3 MO	6 MO	2 YR	3 MO	6 MO	2 YR	3 MO	6 MO	2 YR	3 MO	6 MO	2 YR	3 MO	6 MO	2 YR	3 MO	6 MO	2 YR
Fentanyl	Duragesic 72-Hour Patch	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1
Fentanyl	Fentanyl 72-Hour Patch	555	647	764	85	87	88	17	20	21	0	0	0	95	99	101	555	647	764
Hydrocodone Bitartrate	Hysingla Abuse-Deterrent 24-Hour Extended Release Tablet	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1
Hydrocodone Bitartrate	Zohydro 12-Hour Extended Release Capsule	2	3	3	0	0	0	0	0	0	0	0	0	0	0	0	2	3	3
Hydrocodone Bitartrate	Zohydro Abuse-Deterrent 12-Hour Extended Release Capsule	2	2	3	0	0	0	0	0	0	0	0	0	0	0	0	2	2	3
Hydromorphone HCl	Exalgo Abuse-Deterrent 24-Hour Extended Release Tablet	7	9	10	0	0	0	0	0	0	0	0	0	0	0	0	7	9	10
Hydromorphone HCl	Hydromorphone Abuse-Deterrent 24-Hour Extended Release Tablet	3	3	5	0	0	0	0	0	0	0	0	0	0	0	0	3	3	5
Methadone HCl	Methadone Concentrate	3	4	4	0	0	0	0	0	0	0	0	0	0	0	0	3	4	4
Methadone HCl	Methadone Solution	9	11	14	0	0	0	1	1	1	0	0	0	1	1	1	9	11	14
Methadone HCl	Methadone Tablet	402	464	549	26	26	27	6	7	7	0	0	0	30	31	32	402	464	549
Methadone HCl	Methadose Concentrate	2	3	6	0	0	0	0	0	0	0	0	0	0	0	0	2	3	6
Morphine Sulfate	Kadian 24-Hour Extended Release Capsule	12	18	25	0	0	1	0	0	1	0	0	0	0	0	1	12	18	25
Morphine Sulfate	Morphine Sulfate 24-Hour Extended Release Capsule	1	2	2	0	0	0	1	1	1	0	0	0	1	1	1	1	2	2
Morphine Sulfate	Morphine Sulfate 24-Hour Extended Release Tablet	1,183	1,362	1,633	113	123	130	45	47	47	1	1	2	147	157	165	1,183	1,362	1,633
Morphine Sulfate	MS Contin 24-Hour Extended Release Tablet	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Morphine Sulfate Beads	Avinza 24-Hour Extended Release Capsule	0	1	3	0	0	0	0	0	0	0	0	0	0	0	0	0	1	3
Morphine Sulfate Beads	Morphine Sulfate 24-Hour Extended Release Capsule	1	2	2	0	0	0	1	1	1	0	0	0	1	1	1	1	2	2
Oxycodone HCl	Oxycodone Abuse-Deterrent 12-Hour Extended Release Tablet	14	20	25	0	0	0	4	4	5	0	0	0	4	4	5	14	20	25

CANCER AND SICKLE DIAGNOSES - ALL LONG ACTING OPIOID CLAIMS

GENERIC	DESCRIPTION	A) Cancer History			B) Cancer Pain			C) Palliative Care			D) Sickle Cell Disease			B, C or D			A, B, C or D		
		3 MO	6 MO	2 YR	3 MO	6 MO	2 YR	3 MO	6 MO	2 YR	3 MO	6 MO	2 YR	3 MO	6 MO	2 YR	3 MO	6 MO	2 YR
Oxycodone HCl	Oxycontin Abuse-Deterrent 12-Hour Extended Release Tablet	257	295	348	27	31	33	15	15	15	2	2	2	44	48	50	257	295	348
Oxycodone-Acetaminophen	Xartemis 12-Hour Extended Release Tablet	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
Oxymorphone HCl	Opana 12-Hour Extended Release Tablet	4	6	7	1	1	1	0	0	0	0	0	0	1	1	1	4	6	7
Oxymorphone HCl	Opana Abuse-Deterrent 12-Hour Extended Release Tablet	62	88	123	3	3	3	3	3	3	0	0	0	6	6	6	62	88	123
Oxymorphone HCl	Oxymorphone 12-Hour Extended Release Tablet	76	97	129	3	3	3	2	2	2	3	4	4	7	8	8	76	97	129
Tapentadol HCl	Nucynta 12-Hour Extended Release Tablet	26	31	38	1	1	1	0	0	0	0	0	0	1	1	1	26	31	38
Tramadol HCl	Ryzolt 24-Hour Extended Release Tablet	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Tramadol HCl	Tramadol 24-Hour Extended Release Tablet	53	76	98	3	3	3	1	1	1	0	0	0	4	4	4	53	76	98
Tramadol HCl	Ultram 24-Hour Extended Release Tablet	20	27	35	1	1	2	0	0	0	0	0	0	1	1	2	20	27	35
SUM OF PATIENTS		2,696	3,174	3,829	263	279	292	96	102	105	6	7	8	343	363	379	2,696	3,174	3,829
TOTAL UNIQUE PATIENTS		2,272	2,559	2,971	213	225	235	88	91	92	5	6	7	284	299	311	2,272	2,559	2,971

Units dispensed without excluding patients with cancer/sickle cell disease

TRANSDERMAL - ALL PATIENTS

GENERIC	DESCRIPTION	TOTAL CLAIMS				TOTAL PATIENTS			
		<12	12-15	>15	<12	12-15	>15		
Fentanyl	Duragesic 72-Hour Patch	70	69	1	0	2	2	1	0
Fentanyl	Fentanyl 72-Hour Patch	12,058	9,125	2,886	47	1,480	1,394	259	8
TOTALS		12,128	9,194	2,887	47	1,480	1,394	259	8

SOLID AND LIQUID - ALL PATIENTS

GENERIC	DESCRIPTION	TOTAL CLAIMS				TOTAL PATIENTS					
		<31	31-60	61-90	>90	<31	31-60	61-90	>90		
Hydrocodone Bitartrate	Hysingla Abuse-Deterrent 24-Hour Extended Release Tablet	40	40	0	0	6	6	0	0	0	
Hydrocodone Bitartrate	Zohydro 12-Hour Extended Release Capsule	20	1	16	0	3	6	1	6	0	1
Hydrocodone Bitartrate	Zohydro Abuse-Deterrent 12-Hour Extended Release Capsule	25	1	13	0	11	6	1	5	0	1
Hydromorphone HCl	Exalgo Abuse-Deterrent 24-Hour Extended Release Tablet	109	73	36	0	0	17	13	8	0	0
Hydromorphone HCl	Hydromorphone Abuse-Deterrent 24-Hour Extended Release Tablet	52	32	20	0	0	6	5	2	0	0
Methadone HCl	Methadone Concentrate	107	34	3	5	65	10	6	2	2	5
Methadone HCl	Methadone Solution	205	64	12	9	120	52	30	5	6	19
Methadone HCl	Methadone Tablet	13,037	1,311	2,595	2,647	6,484	1,248	420	547	468	613
Methadone HCl	Methadose Concentrate	23	10	2	0	11	9	4	2	0	6
Morphine Sulfate	Kadian 24-Hour Extended Release Capsule	320	112	187	21	0	50	30	26	8	0
Morphine Sulfate	Morphine Sulfate 24-Hour Extended Release Capsule	551	245	271	35	0	112	69	57	11	0
Morphine Sulfate	Morphine Sulfate 24-Hour Extended Release Tablet	31,624	6,037	14,848	10,416	323	3,454	1,670	2,346	1,181	68

Morphine Sulfate	MS Contin 24-Hour Extended Release Tablet	2	0	2	0	0	2	0	2	0	0
Morphine Sulfate Beads	Avinza 24-Hour Extended Release Capsule	99	99	0	0	0	8	8	0	0	0
Morphine Sulfate Beads	Morphine Sulfate 24-Hour Extended Release Capsule	46	36	10	0	0	6	5	1	0	0
Oxycodone HCl	Oxycodone Abuse-Deterrent 12-Hour Extended Release Tablet	332	27	116	172	17	80	19	42	32	4
Oxycodone HCl	Oxycontin Abuse-Deterrent 12-Hour Extended Release Tablet	8,476	921	4,453	2,956	146	704	259	525	209	20
Oxycodone-Acetaminophen	Xartemis 12-Hour Extended Release Tablet	1	0	0	0	1	1	0	0	0	1
Oxymorphone HCl	Opana 12-Hour Extended Release Tablet	22	7	13	2	0	18	7	9	2	0
Oxymorphone HCl	Opana Abuse-Deterrent 12-Hour Extended Release Tablet	1,362	228	924	194	16	315	124	236	44	4
Oxymorphone HCl	Oxymorphone 12-Hour Extended Release Tablet	2,381	308	1,420	625	28	298	128	231	64	3
Tapentadol HCl	Nucynta 12-Hour Extended Release Tablet	451	68	376	7	0	88	26	74	5	0
Tramadol HCl	Ryzolt 24-Hour Extended Release Tablet	2	2	0	0	0	2	2	0	0	0
Tramadol HCl	Tramadol 24-Hour Extended Release Tablet	1,202	1,083	100	9	10	209	188	30	6	3
Tramadol HCl	Ultram 24-Hour Extended Release Tablet	318	248	56	3	11	73	61	13	2	1
TOTALS		60,807	10,987	25,473	17,101	7,246	5,395	2,694	3,501	1,875	728

Units dispensed excluding potential patients with cancer/sickle cell disease

TRANSDERMAL – CANCER/SICKLE CELL PATIENTS EXCLUDED		TOTAL				TOTAL			
GENERIC	DESCRIPTION	CLAIMS	<12	12-15	>15	PATIENTS	<12	12-15	>15
Fentanyl	Duragesic 72-Hour Patch	1	1	0	0	1	1	0	0
Fentanyl	Fentanyl 72-Hour Patch	4,550	3,566	982	2	721	676	118	1
TOTALS		4,551	3,567	982	2	721	676	118	1

SOLID AND LIQUID – CANCER/SICKLE CELL PATIENTS EXCLUDED		TOTAL				TOTAL					
GENERIC	DESCRIPTION	CLAIMS	<31	31-60	61-90	>90	PATIENTS	<31	31-60	61-90	>90
Hydrocodone Bitartrate	Hysingla Abuse-Deterrent 24-Hour Extended Release Tablet	9	9	0	0	0	3	3	0	0	0
Hydrocodone Bitartrate	Zohydro 12-Hour Extended Release Capsule	3	0	3	0	0	3	0	3	0	0
Hydrocodone Bitartrate	Zohydro Abuse-Deterrent 12-Hour Extended Release Capsule	10	0	10	0	0	3	0	3	0	0
Hydromorphone HCl	Exalgo Abuse-Deterrent 24-Hour Extended Release Tablet	13	7	6	0	0	6	3	4	0	0
Hydromorphone HCl	Hydromorphone Abuse-Deterrent 24-Hour Extended Release Tablet	0	0	0	0	0	0	0	0	0	0
Methadone HCl	Methadone Concentrate	43	30	1	0	12	6	4	1	0	2
Methadone HCl	Methadone Solution	113	59	12	5	37	38	26	5	3	11
Methadone HCl	Methadone Tablet	5,984	581	1,033	1,202	3,168	741	228	303	248	363
Methadone HCl	Methadose Concentrate	10	8	0	0	2	3	2	0	0	2
Morphine Sulfate	Kadian 24-Hour Extended Release Capsule	86	55	25	6	0	21	12	10	3	0
Morphine Sulfate	Morphine Sulfate 24-Hour Extended Release Capsule	190	64	112	14	0	47	28	26	2	0
Morphine Sulfate	Morphine Sulfate 24-Hour Extended Release Tablet	13,426	2,753	6,509	4,084	80	1,950	926	1,245	564	23

Morphine Sulfate	MS Contin 24-Hour Extended Release Tablet	2	0	2	0	0	2	0	2	0	0
Morphine Sulfate Beads	Avinza 24-Hour Extended Release Capsule	65	65	0	0	0	3	3	0	0	0
Morphine Sulfate Beads	Morphine Sulfate 24-Hour Extended Release Capsule	8	8	0	0	0	3	3	0	0	0
Oxycodone HCl	Oxycodone Abuse-Deterrent 12-Hour Extended Release Tablet	148	19	59	66	4	41	14	22	13	1
Oxycodone HCl	Oxycontin Abuse-Deterrent 12-Hour Extended Release Tablet	3,443	403	1,713	1,308	19	348	129	251	93	3
Oxycodone-Acetaminophen	Xartemis 12-Hour Extended Release Tablet	0	0	0	0	0	0	0	0	0	0
Oxymorphone HCl	Opana 12-Hour Extended Release Tablet	9	3	4	2	0	8	3	3	2	0
Oxymorphone HCl	Opana Abuse-Deterrent 12-Hour Extended Release Tablet	646	123	436	74	13	181	70	135	20	1
Oxymorphone HCl	Oxymorphone 12-Hour Extended Release Tablet	1,110	159	714	216	21	159	69	121	28	1
Tapentadol HCl	Nucynta 12-Hour Extended Release Tablet	176	20	152	4	0	44	10	38	2	0
Tramadol HCl	Ryzolt 24-Hour Extended Release Tablet	2	2	0	0	0	2	2	0	0	0
Tramadol HCl	Tramadol 24-Hour Extended Release Tablet	499	434	57	7	1	126	108	17	4	1
Tramadol HCl	Ultram 24-Hour Extended Release Tablet	125	73	40	1	11	42	34	6	1	1
TOTALS		26,120	4,875	10,888	6,989	3,368	3,142	1,509	1,885	929	404

Proposed Quantity Limits & patients/claims falling outside the limits

ALL PATIENTS			Claims			Patients		
Agent	Product Description	Proposed QL	2013-2016	Exceeding PQL	Percent	2013-2016	Exceeding PQL	Percent
Fentanyl	DURAGESIC DIS 100MCG/H	11	0	0	NA	0	0	NA
Fentanyl	DURAGESIC DIS 12MCG/HR	11	0	0	NA	0	0	NA
Fentanyl	DURAGESIC DIS 25MCG/HR	11	0	0	NA	0	0	NA
Fentanyl	DURAGESIC DIS 50MCG/HR	11	1	0	0.00%	1	0	0.00%
Fentanyl	DURAGESIC DIS 75MCG/HR	11	69	1	1.45%	1	1	100.00%
Fentanyl	FENTANYL DIS 100MCG/H	11	939	331	35.25%	116	34	29.31%
Fentanyl	FENTANYL DIS 12MCG/HR	11	1214	124	10.21%	462	29	6.28%
Fentanyl	FENTANYL DIS 25MCG/HR	11	3175	564	17.76%	822	88	10.71%
Fentanyl	FENTANYL DIS 37.5MCG	11	40	1	2.50%	12	1	8.33%
Fentanyl	FENTANYL DIS 50MCG/HR	11	3200	760	23.75%	585	116	19.83%
Fentanyl	FENTANYL DIS 62.5MCG	11	0	0	NA	0	0	NA
Fentanyl	FENTANYL DIS 75MCG/HR	11	3490	1153	33.04%	353	99	28.05%
Fentanyl	FENTANYL DIS 87.5MCG	11	0	0	NA	0	0	NA
Hydrocodone Bitartrate	HYSINGLA ER TAB 100 MG	60	1	0	0.00%	1	0	0.00%
Hydrocodone Bitartrate	HYSINGLA ER TAB 120 MG	60	0	0	NA	0	0	NA
Hydrocodone Bitartrate	HYSINGLA ER TAB 20 MG	60	1	0	0.00%	1	0	0.00%
Hydrocodone Bitartrate	HYSINGLA ER TAB 30 MG	60	0	0	NA	0	0	NA
Hydrocodone Bitartrate	HYSINGLA ER TAB 40 MG	60	9	0	0.00%	1	0	0.00%
Hydrocodone Bitartrate	HYSINGLA ER TAB 60 MG	60	17	0	0.00%	3	0	0.00%
Hydrocodone Bitartrate	HYSINGLA ER TAB 80 MG	60	12	0	0.00%	3	0	0.00%
Hydrocodone Bitartrate	ZOHYDRO ER CAP 10MG	60	1	0	0.00%	1	0	0.00%
Hydrocodone Bitartrate	ZOHYDRO ER CAP 15MG	60	3	0	0.00%	3	0	0.00%
Hydrocodone Bitartrate	ZOHYDRO ER CAP 20MG	60	11	0	0.00%	5	0	0.00%
Hydrocodone Bitartrate	ZOHYDRO ER CAP 30MG	60	8	0	0.00%	2	0	0.00%
Hydrocodone Bitartrate	ZOHYDRO ER CAP 40MG	60	0	0	NA	0	0	NA
Hydrocodone Bitartrate	ZOHYDRO ER CAP 50MG	60	22	14	63.64%	1	1	100.00%
Hydromorphone HCl	EXALGO TAB 12MG	30	37	16	43.24%	9	3	33.33%
Hydromorphone HCl	EXALGO TAB 16MG	30	30	6	20.00%	7	4	57.14%
Hydromorphone HCl	EXALGO TAB 32MG	30	19	12	63.16%	3	1	33.33%
Hydromorphone HCl	EXALGO TAB 8MG	30	23	2	8.70%	7	2	28.57%
Hydromorphone HCl	HYDROMORPHON TAB 12MG ER	30	11	5	45.45%	3	2	66.67%
Hydromorphone HCl	HYDROMORPHON TAB 16MG ER	30	25	15	60.00%	4	2	50.00%

ALL PATIENTS			Claims			Patients		
Agent	Product Description	Proposed QL	2013-2016	Exceeding PQL	Percent	2013-2016	Exceeding PQL	Percent
Hydromorphone HCl	HYDROMORPHON TAB 32MG ER	30	15	0	0.00%	1	0	0.00%
Hydromorphone HCl	HYDROMORPHON TAB 8MG ER	30	1	0	0.00%	1	0	0.00%
Methadone HCl	DOLOPHINE TAB 10MG	60	0	0	NA	0	0	NA
Methadone HCl	DOLOPHINE TAB 5MG	60	0	0	NA	0	0	NA
Methadone HCl	METHADONE TAB 10MG	60	11366	8532	75.07%	1046	781	74.67%
Methadone HCl	METHADONE TAB 40MG	30	0	0	NA	0	0	NA
Methadone HCl	METHADONE TAB 5MG	60	1671	599	35.85%	350	129	36.86%
Methadone HCl	METHADOSE TAB 40MG	30	0	0	NA	0	0	NA
Morphine Sulfate	KADIAN CAP 100MG ER	60	2	0	0.00%	2	0	0.00%
Morphine Sulfate	KADIAN CAP 10MG ER	60	4	0	0.00%	3	0	0.00%
Morphine Sulfate	KADIAN CAP 130MG ER	60	21	0	0.00%	1	0	0.00%
Morphine Sulfate	KADIAN CAP 150MG ER	60	0	0	NA	0	0	NA
Morphine Sulfate	KADIAN CAP 200MG ER	60	43	0	0.00%	1	0	0.00%
Morphine Sulfate	KADIAN CAP 20MG ER	60	62	16	25.81%	21	4	19.05%
Morphine Sulfate	KADIAN CAP 30MG ER	60	66	2	3.03%	17	2	11.76%
Morphine Sulfate	KADIAN CAP 40MG ER	60	52	0	0.00%	5	0	0.00%
Morphine Sulfate	KADIAN CAP 50MG ER	60	22	0	0.00%	3	0	0.00%
Morphine Sulfate	KADIAN CAP 60MG ER	60	37	1	2.70%	7	1	14.29%
Morphine Sulfate	KADIAN CAP 70MG ER	60	2	0	0.00%	1	0	0.00%
Morphine Sulfate	KADIAN CAP 80MG ER	60	9	2	22.22%	3	1	33.33%
Morphine Sulfate	MORPHINE SUL CAP 100MG ER	60	70	1	1.43%	10	1	10.00%
Morphine Sulfate	MORPHINE SUL CAP 10MG ER	60	3	0	0.00%	3	0	0.00%
Morphine Sulfate	MORPHINE SUL CAP 20MG ER	60	125	13	10.40%	46	3	6.52%
Morphine Sulfate	MORPHINE SUL CAP 30MG ER	60	172	5	2.90%	42	3	7.14%
Morphine Sulfate	MORPHINE SUL CAP 50MG ER	60	81	2	2.47%	21	2	9.52%
Morphine Sulfate	MORPHINE SUL CAP 60MG ER	60	43	0	0.00%	10	0	0.00%
Morphine Sulfate	MORPHINE SUL CAP 80MG ER	60	57	14	24.56%	9	2	22.22%
Morphine Sulfate	MORPHINE SUL TAB 100MG CR	90	0	0	NA	0	0	NA
Morphine Sulfate	MORPHINE SUL TAB 100MG ER	90	2644	117	4.43%	207	12	5.80%
Morphine Sulfate	MORPHINE SUL TAB 15MG CR	90	0	0	NA	0	0	NA
Morphine Sulfate	MORPHINE SUL TAB 15MG ER	90	10033	40	0.40%	2221	19	0.86%
Morphine Sulfate	MORPHINE SUL TAB 200MG ER	90	209	1	0.48%	18	1	5.56%
Morphine Sulfate	MORPHINE SUL TAB 30MG ER	90	12181	115	0.94%	1635	31	1.90%
Morphine Sulfate	MORPHINE SUL TAB 60MG CR	90	0	0	NA	0	0	NA

ALL PATIENTS			Claims			Patients		
Agent	Product Description	Proposed QL	2013-2016	Exceeding PQL	Percent	2013-2016	Exceeding PQL	Percent
Morphine Sulfate	MORPHINE SUL TAB 60MG ER	90	6557	50	0.76%	646	11	1.70%
Morphine Sulfate	MS CONTIN TAB 100MG CR	90	1	0	0.00%	1	0	0.00%
Morphine Sulfate	MS CONTIN TAB 15MG CR	90	1	0	0.00%	1	0	0.00%
Morphine Sulfate	MS CONTIN TAB 200MG CR	90	0	0	NA	0	0	NA
Morphine Sulfate	MS CONTIN TAB 30MG CR	90	0	0	NA	0	0	NA
Morphine Sulfate	MS CONTIN TAB 60MG CR	90	0	0	NA	0	0	NA
Morphine Sulfate Beads	AVINZA CAP 120MG	30	39	0	0.00%	2	0	0.00%
Morphine Sulfate Beads	AVINZA CAP 30MG	30	25	0	0.00%	1	0	0.00%
Morphine Sulfate Beads	AVINZA CAP 45MG	30	3	0	0.00%	1	0	0.00%
Morphine Sulfate Beads	AVINZA CAP 60MG	30	28	0	0.00%	5	0	0.00%
Morphine Sulfate Beads	AVINZA CAP 75MG	30	3	0	0.00%	1	0	0.00%
Morphine Sulfate Beads	AVINZA CAP 90MG	30	1	0	0.00%	1	0	0.00%
Morphine Sulfate Beads	MORPHINE SUL CAP 120MG ER	30	7	0	0.00%	2	0	0.00%
Morphine Sulfate Beads	MORPHINE SUL CAP 30MG ER	30	10	10	100.00%	1	1	100.00%
Morphine Sulfate Beads	MORPHINE SUL CAP 45MG ER	30	2	0	0.00%	2	0	0.00%
Morphine Sulfate Beads	MORPHINE SUL CAP 60MG ER	30	0	0	NA	0	0	NA
Morphine Sulfate Beads	MORPHINE SUL CAP 75MG ER	30	27	0	0.00%	1	0	0.00%
Morphine Sulfate Beads	MORPHINE SUL CAP 90MG ER	30	0	0	NA	0	0	NA
Oxycodone HCl	OXYCODONE TAB 10MG ER	60	36	8	22.22%	21	1	4.76%
Oxycodone HCl	OXYCODONE TAB 15MG ER	60	0	0	NA	0	0	NA
Oxycodone HCl	OXYCODONE TAB 20MG ER	60	31	4	12.90%	12	1	8.33%
Oxycodone HCl	OXYCODONE TAB 40MG ER	60	137	93	67.88%	30	20	66.67%
Oxycodone HCl	OXYCODONE TAB 60MG ER	60	0	0	NA	0	0	NA
Oxycodone HCl	OXYCODONE TAB 80MG ER	60	128	84	65.63%	21	14	66.67%
Oxycodone HCl	OXYCODONE TAB ER 30MG	60	0	0	NA	0	0	NA
Oxycodone HCl	OXYCONTIN TAB 10MG CR	60	545	101	18.53%	137	18	13.14%
Oxycodone HCl	OXYCONTIN TAB 15MG CR	60	581	49	8.43%	120	8	6.67%
Oxycodone HCl	OXYCONTIN TAB 20MG CR	60	1507	479	31.79%	232	51	21.98%
Oxycodone HCl	OXYCONTIN TAB 30MG CR	60	1452	333	22.93%	191	46	24.08%
Oxycodone HCl	OXYCONTIN TAB 40MG CR	60	1753	812	46.32%	173	71	41.04%
Oxycodone HCl	OXYCONTIN TAB 60MG CR	60	1096	499	45.53%	105	40	38.10%
Oxycodone HCl	OXYCONTIN TAB 80MG CR	60	1542	829	53.76%	95	53	55.79%
Oxycodone-Acetaminophen	XARTEMIS XR TAB 7.5-325	120	1	0	0.00%	1	0	0.00%
Oxymorphone HCl	OPANA ER TAB 10MG	60	325	35	10.77%	123	9	7.32%

ALL PATIENTS			Claims			Patients		
Agent	Product Description	Proposed QL	2013-2016	Exceeding PQL	Percent	2013-2016	Exceeding PQL	Percent
Oxymorphone HCl	OPANA ER TAB 15MG	60	388	80	20.62%	122	27	22.13%
Oxymorphone HCl	OPANA ER TAB 20MG	60	226	62	27.43%	43	4	9.30%
Oxymorphone HCl	OPANA ER TAB 30MG	60	150	6	4.00%	32	2	6.25%
Oxymorphone HCl	OPANA ER TAB 40MG	60	201	26	12.94%	28	8	28.57%
Oxymorphone HCl	OPANA ER TAB 5MG	60	69	3	4.35%	35	2	5.71%
Oxymorphone HCl	OPANA ER TAB 7.5MG	60	25	0	0.00%	14	0	0.00%
Oxymorphone HCl	OXYMORPHONE TAB 10MG ER	60	191	21	10.99%	67	4	5.97%
Oxymorphone HCl	OXYMORPHONE TAB 15MG ER	60	403	78	19.35%	97	17	17.53%
Oxymorphone HCl	OXYMORPHONE TAB 20MG ER	60	473	97	20.51%	92	16	17.39%
Oxymorphone HCl	OXYMORPHONE TAB 30MG ER	60	553	126	22.78%	78	21	26.92%
Oxymorphone HCl	OXYMORPHONE TAB 40MG ER	60	663	330	49.77%	57	20	35.09%
Oxymorphone HCl	OXYMORPHONE TAB 5MG ER	60	53	1	1.89%	26	1	3.85%
Oxymorphone HCl	OXYMORPHONE TAB 7.5MG ER	60	45	0	0.00%	18	0	0.00%
Tapentadol HCl	NUCYNTA ER TAB 100MG	60	192	6	3.13%	53	4	7.55%
Tapentadol HCl	NUCYNTA ER TAB 150MG	60	60	0	0.00%	28	0	0.00%
Tapentadol HCl	NUCYNTA ER TAB 200MG	60	62	0	0.00%	15	0	0.00%
Tapentadol HCl	NUCYNTA ER TAB 250MG	60	88	0	0.00%	7	0	0.00%
Tapentadol HCl	NUCYNTA ER TAB 50MG	60	49	1	2.04%	26	1	3.85%
Tramadol HCl	CONZIP CAP 100MG	30	0	0	NA	0	0	NA
Tramadol HCl	CONZIP CAP 200MG	30	0	0	NA	0	0	NA
Tramadol HCl	CONZIP CAP 300MG	30	0	0	NA	0	0	NA
Tramadol HCl	TRAMADOL HCL CAP 150MG ER	30	0	0	NA	0	0	NA
Tramadol HCl	TRAMADOL HCL CAP ER 100MG	30	0	0	NA	0	0	NA
Tramadol HCl	TRAMADOL HCL CAP ER 200MG	30	0	0	NA	0	0	NA
Tramadol HCl	TRAMADOL HCL CAP ER 300MG	30	0	0	NA	0	0	NA
Tramadol HCl	TRAMADOL HCL TAB 100MG ER	30	430	98	22.79%	97	30	30.93%
Tramadol HCl	TRAMADOL HCL TAB 200MG ER	30	424	16	3.77%	70	4	5.71%
Tramadol HCl	TRAMADOL HCL TAB 300MG ER	30	348	5	1.44%	66	1	1.52%
Tramadol HCl	ULTRAM ER TAB 100MG	30	117	34	29.06%	42	12	28.57%
Tramadol HCl	ULTRAM ER TAB 200MG	30	101	5	4.95%	23	2	8.70%
Tramadol HCl	ULTRAM ER TAB 300MG	30	100	31	31.00%	13	1	7.69%

POTENTIAL PATIENTS WITH CANCER/SICKLE CELL DISEASE EXCLUDED			Claims			Patients		
Agent	Product Description	Proposed QL	2013-2016	Exceeding PQL	Percent	2013-2016	Exceeding PQL	Percent
Fentanyl	DURAGESIC DIS 100MCG/H	11	0	0	NA	0	0	NA
Fentanyl	DURAGESIC DIS 12MCG/HR	11	0	0	NA	0	0	NA
Fentanyl	DURAGESIC DIS 25MCG/HR	11	0	0	NA	0	0	NA
Fentanyl	DURAGESIC DIS 50MCG/HR	11	1	0	0.00%	1	0	0.00%
Fentanyl	DURAGESIC DIS 75MCG/HR	11	0	0	NA	0	0	NA
Fentanyl	FENTANYL DIS 100MCG/H	11	206	83	40.29%	26	6	23.08%
Fentanyl	FENTANYL DIS 12MCG/HR	11	590	67	11.36%	234	16	6.84%
Fentanyl	FENTANYL DIS 25MCG/HR	11	1217	184	15.12%	379	38	10.03%
Fentanyl	FENTANYL DIS 37.5MCG	11	19	0	0.00%	4	0	0.00%
Fentanyl	FENTANYL DIS 50MCG/HR	11	1403	363	25.87%	266	61	22.93%
Fentanyl	FENTANYL DIS 62.5MCG	11	0	0	NA	0	0	NA
Fentanyl	FENTANYL DIS 75MCG/HR	11	1115	287	25.74%	143	35	24.48%
Fentanyl	FENTANYL DIS 87.5MCG	11	0	0	NA	0	0	NA
Hydrocodone Bitartrate	HYSINGLA ER TAB 100 MG	60	1	0	0.00%	1	0	0.00%
Hydrocodone Bitartrate	HYSINGLA ER TAB 120 MG	60	0	0	NA	0	0	NA
Hydrocodone Bitartrate	HYSINGLA ER TAB 20 MG	60	0	0	NA	0	0	NA
Hydrocodone Bitartrate	HYSINGLA ER TAB 30 MG	60	0	0	NA	0	0	NA
Hydrocodone Bitartrate	HYSINGLA ER TAB 40 MG	60	0	0	NA	0	0	NA
Hydrocodone Bitartrate	HYSINGLA ER TAB 60 MG	60	2	0	0.00%	2	0	0.00%
Hydrocodone Bitartrate	HYSINGLA ER TAB 80 MG	60	6	0	0.00%	2	0	0.00%
Hydrocodone Bitartrate	ZOHYDRO ER CAP 10MG	60	0	0	NA	0	0	NA
Hydrocodone Bitartrate	ZOHYDRO ER CAP 15MG	60	2	0	0.00%	2	0	0.00%
Hydrocodone Bitartrate	ZOHYDRO ER CAP 20MG	60	11	0	0.00%	5	0	0.00%
Hydrocodone Bitartrate	ZOHYDRO ER CAP 30MG	60	0	0	NA	0	0	NA
Hydrocodone Bitartrate	ZOHYDRO ER CAP 40MG	60	0	0	NA	0	0	NA
Hydrocodone Bitartrate	ZOHYDRO ER CAP 50MG	60	0	0	NA	0	0	NA
Hydromorphone HCl	EXALGO TAB 12MG	30	3	0	0.00%	2	0	0.00%
Hydromorphone HCl	EXALGO TAB 16MG	30	6	5	83.33%	3	3	100.00%
Hydromorphone HCl	EXALGO TAB 32MG	30	0	0	NA	0	0	NA
Hydromorphone HCl	EXALGO TAB 8MG	30	4	1	25.00%	3	1	33.33%
Hydromorphone HCl	HYDROMORPHON TAB 12MG ER	30	0	0	NA	0	0	NA
Hydromorphone HCl	HYDROMORPHON TAB 16MG ER	30	0	0	NA	0	0	NA
Hydromorphone HCl	HYDROMORPHON TAB 32MG ER	30	0	0	NA	0	0	NA
Hydromorphone HCl	HYDROMORPHON TAB 8MG ER	30	0	0	NA	0	0	NA

POTENTIAL PATIENTS WITH CANCER/SICKLE CELL DISEASE EXCLUDED			Claims	Exceeding		Patients	Exceeding	
Agent	Product Description	Proposed QL	2013-2016	PQL	Percent	2013-2016	PQL	Percent
Methadone HCl	DOLOPHINE TAB 10MG	60	0	0	NA	0	0	NA
Methadone HCl	DOLOPHINE TAB 5MG	60	0	0	NA	0	0	NA
Methadone HCl	METHADONE TAB 10MG	60	5193	4076	78.49%	620	464	74.84%
Methadone HCl	METHADONE TAB 40MG	30	0	0	NA	0	0	NA
Methadone HCl	METHADONE TAB 5MG	60	791	294	37.17%	191	60	31.41%
Methadone HCl	METHADOSE TAB 40MG	30	0	0	NA	0	0	NA
Morphine Sulfate	KADIAN CAP 100MG ER	60	0	0	NA	0	0	NA
Morphine Sulfate	KADIAN CAP 10MG ER	60	2	0	0.00%	1	0	0.00%
Morphine Sulfate	KADIAN CAP 130MG ER	60	21	0	0.00%	1	0	0.00%
Morphine Sulfate	KADIAN CAP 150MG ER	60	0	0	NA	0	0	NA
Morphine Sulfate	KADIAN CAP 200MG ER	60	0	0	NA	0	0	NA
Morphine Sulfate	KADIAN CAP 20MG ER	60	15	4	26.67%	10	2	20.00%
Morphine Sulfate	KADIAN CAP 30MG ER	60	21	0	0.00%	6	0	0.00%
Morphine Sulfate	KADIAN CAP 40MG ER	60	22	0	0.00%	3	0	0.00%
Morphine Sulfate	KADIAN CAP 50MG ER	60	0	0	NA	0	0	NA
Morphine Sulfate	KADIAN CAP 60MG ER	60	1	0	0.00%	1	0	0.00%
Morphine Sulfate	KADIAN CAP 70MG ER	60	0	0	NA	0	0	NA
Morphine Sulfate	KADIAN CAP 80MG ER	60	4	2	50.00%	1	1	100.00%
Morphine Sulfate	MORPHINE SUL CAP 100MG ER	60	8	1	12.50%	5	1	20.00%
Morphine Sulfate	MORPHINE SUL CAP 10MG ER	60	3	0	0.00%	3	0	0.00%
Morphine Sulfate	MORPHINE SUL CAP 20MG ER	60	33	0	0.00%	17	0	0.00%
Morphine Sulfate	MORPHINE SUL CAP 30MG ER	60	61	0	0.00%	14	0	0.00%
Morphine Sulfate	MORPHINE SUL CAP 50MG ER	60	44	0	0.00%	10	0	0.00%
Morphine Sulfate	MORPHINE SUL CAP 60MG ER	60	9	0	0.00%	5	0	0.00%
Morphine Sulfate	MORPHINE SUL CAP 80MG ER	60	32	13	40.63%	3	1	33.33%
Morphine Sulfate	MORPHINE SUL TAB 100MG CR	90	0	0	NA	0	0	NA
Morphine Sulfate	MORPHINE SUL TAB 100MG ER	90	1157	36	3.11%	89	5	5.62%
Morphine Sulfate	MORPHINE SUL TAB 15MG CR	90	0	0	NA	0	0	NA
Morphine Sulfate	MORPHINE SUL TAB 15MG ER	90	4580	10	0.22%	1259	5	0.40%
Morphine Sulfate	MORPHINE SUL TAB 200MG ER	90	33	0	0.00%	5	0	0.00%
Morphine Sulfate	MORPHINE SUL TAB 30MG ER	90	5123	24	0.47%	854	11	1.29%
Morphine Sulfate	MORPHINE SUL TAB 60MG CR	90	0	0	NA	0	0	NA
Morphine Sulfate	MORPHINE SUL TAB 60MG ER	90	2533	10	0.39%	309	3	0.97%
Morphine Sulfate	MS CONTIN TAB 100MG CR	90	1	0	0.00%	1	0	0.00%

POTENTIAL PATIENTS WITH CANCER/SICKLE CELL DISEASE EXCLUDED			Claims			Patients		
Agent	Product Description	Proposed QL	2013-2016	Exceeding PQL	Percent	2013-2016	Exceeding PQL	Percent
Morphine Sulfate	MS CONTIN TAB 15MG CR	90	1	0	0.00%	1	0	0.00%
Morphine Sulfate	MS CONTIN TAB 200MG CR	90	0	0	NA	0	0	NA
Morphine Sulfate	MS CONTIN TAB 30MG CR	90	0	0	NA	0	0	NA
Morphine Sulfate	MS CONTIN TAB 60MG CR	90	0	0	NA	0	0	NA
Morphine Sulfate Beads	AVINZA CAP 120MG	30	39	0	0.00%	2	0	0.00%
Morphine Sulfate Beads	AVINZA CAP 30MG	30	25	0	0.00%	1	0	0.00%
Morphine Sulfate Beads	AVINZA CAP 45MG	30	0	0	NA	0	0	NA
Morphine Sulfate Beads	AVINZA CAP 60MG	30	1	0	0.00%	1	0	0.00%
Morphine Sulfate Beads	AVINZA CAP 75MG	30	0	0	NA	0	0	NA
Morphine Sulfate Beads	AVINZA CAP 90MG	30	0	0	NA	0	0	NA
Morphine Sulfate Beads	MORPHINE SUL CAP 120MG ER	30	7	0	0.00%	2	0	0.00%
Morphine Sulfate Beads	MORPHINE SUL CAP 30MG ER	30	0	0	NA	0	0	NA
Morphine Sulfate Beads	MORPHINE SUL CAP 45MG ER	30	1	0	0.00%	1	0	0.00%
Morphine Sulfate Beads	MORPHINE SUL CAP 60MG ER	30	0	0	NA	0	0	NA
Morphine Sulfate Beads	MORPHINE SUL CAP 75MG ER	30	0	0	NA	0	0	NA
Morphine Sulfate Beads	MORPHINE SUL CAP 90MG ER	30	0	0	NA	0	0	NA
Oxycodone HCl	OXYCODONE TAB 10MG ER	60	18	0	0.00%	14	0	0.00%
Oxycodone HCl	OXYCODONE TAB 15MG ER	60	0	0	NA	0	0	NA
Oxycodone HCl	OXYCODONE TAB 20MG ER	60	19	4	21.05%	8	1	12.50%
Oxycodone HCl	OXYCODONE TAB 40MG ER	60	73	54	73.97%	15	10	66.67%
Oxycodone HCl	OXYCODONE TAB 60MG ER	60	0	0	NA	0	0	NA
Oxycodone HCl	OXYCODONE TAB 80MG ER	60	38	12	31.58%	7	3	42.86%
Oxycodone HCl	OXYCODONE TAB ER 30MG	60	0	0	NA	0	0	NA
Oxycodone HCl	OXYCONTIN TAB 10MG CR	60	201	21	10.45%	68	8	11.76%
Oxycodone HCl	OXYCONTIN TAB 15MG CR	60	294	32	10.88%	59	3	5.08%
Oxycodone HCl	OXYCONTIN TAB 20MG CR	60	615	266	43.25%	110	25	22.73%
Oxycodone HCl	OXYCONTIN TAB 30MG CR	60	660	149	22.58%	89	18	20.22%
Oxycodone HCl	OXYCONTIN TAB 40MG CR	60	746	359	48.12%	88	35	39.77%
Oxycodone HCl	OXYCONTIN TAB 60MG CR	60	308	152	49.35%	44	16	36.36%
Oxycodone HCl	OXYCONTIN TAB 80MG CR	60	619	348	56.22%	37	23	62.16%
Oxycodone-Acetaminophen	XARTEMIS XR TAB 7.5-325	120	0	0	NA	0	0	NA
Oxymorphone HCl	OPANA ER TAB 10MG	60	141	3	2.13%	64	3	4.69%
Oxymorphone HCl	OPANA ER TAB 15MG	60	224	46	20.54%	69	14	20.29%
Oxymorphone HCl	OPANA ER TAB 20MG	60	116	18	15.52%	20	2	10.00%

POTENTIAL PATIENTS WITH CANCER/SICKLE CELL DISEASE EXCLUDED			Claims			Patients		
Agent	Product Description	Proposed QL	2013-2016	Exceeding PQL	Percent	2013-2016	Exceeding PQL	Percent
Oxymorphone HCl	OPANA ER TAB 30MG	60	73	5	6.85%	18	1	5.56%
Oxymorphone HCl	OPANA ER TAB 40MG	60	63	17	26.98%	17	4	23.53%
Oxymorphone HCl	OPANA ER TAB 5MG	60	29	0	0.00%	20	0	0.00%
Oxymorphone HCl	OPANA ER TAB 7.5MG	60	9	0	0.00%	9	0	0.00%
Oxymorphone HCl	OXYMORPHONE TAB 10MG ER	60	82	15	18.29%	34	2	5.88%
Oxymorphone HCl	OXYMORPHONE TAB 15MG ER	60	207	25	12.08%	54	7	12.96%
Oxymorphone HCl	OXYMORPHONE TAB 20MG ER	60	296	44	14.86%	49	6	12.24%
Oxymorphone HCl	OXYMORPHONE TAB 30MG ER	60	233	51	21.89%	39	10	25.64%
Oxymorphone HCl	OXYMORPHONE TAB 40MG ER	60	232	102	43.97%	25	8	32.00%
Oxymorphone HCl	OXYMORPHONE TAB 5MG ER	60	29	0	0.00%	13	0	0.00%
Oxymorphone HCl	OXYMORPHONE TAB 7.5MG ER	60	31	0	0.00%	9	0	0.00%
Tapentadol HCl	NUCYNTA ER TAB 100MG	60	86	4	4.65%	25	2	8.00%
Tapentadol HCl	NUCYNTA ER TAB 150MG	60	24	0	0.00%	12	0	0.00%
Tapentadol HCl	NUCYNTA ER TAB 200MG	60	24	0	0.00%	6	0	0.00%
Tapentadol HCl	NUCYNTA ER TAB 250MG	60	16	0	0.00%	3	0	0.00%
Tapentadol HCl	NUCYNTA ER TAB 50MG	60	26	0	0.00%	15	0	0.00%
Tramadol HCl	CONZIP CAP 100MG	30	0	0	NA	0	0	NA
Tramadol HCl	CONZIP CAP 200MG	30	0	0	NA	0	0	NA
Tramadol HCl	CONZIP CAP 300MG	30	0	0	NA	0	0	NA
Tramadol HCl	TRAMADOL HCL CAP 150MG ER	30	0	0	NA	0	0	NA
Tramadol HCl	TRAMADOL HCL CAP ER 100MG	30	0	0	NA	0	0	NA
Tramadol HCl	TRAMADOL HCL CAP ER 200MG	30	0	0	NA	0	0	NA
Tramadol HCl	TRAMADOL HCL CAP ER 300MG	30	0	0	NA	0	0	NA
Tramadol HCl	TRAMADOL HCL TAB 100MG ER	30	162	45	27.78%	57	18	31.58%
Tramadol HCl	TRAMADOL HCL TAB 200MG ER	30	161	15	9.32%	41	3	7.32%
Tramadol HCl	TRAMADOL HCL TAB 300MG ER	30	176	5	2.84%	42	1	2.38%
Tramadol HCl	ULTRAM ER TAB 100MG	30	63	21	33.33%	28	7	25.00%
Tramadol HCl	ULTRAM ER TAB 200MG	30	18	0	0.00%	10	0	0.00%
Tramadol HCl	ULTRAM ER TAB 300MG	30	44	31	70.45%	5	1	20.00%

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