

ORAL OPIOIDS FOR CHRONIC NON-MALIGNANT PAIN

Introduction

Chronic non-malignant pain (CNMP) is a common cause of disability and is estimated to affect one in five adult Americans.¹ The American Pain Society endorses the use of opioids for refractory chronic non-cancer pain when used according to published guidelines.² Long-acting (LA) opioids are especially useful due to an extended duration of action, dosing convenience, and a tolerable adverse effect profile for most patients.³ **At a recent meeting of the Idaho Pharmacy and Therapeutics Committee, Avinza[®] and Kadian[®] (morphine sulfate extended-release products) and methadone were chosen as the “preferred agents” from the LA opioid class for Medicaid recipients. Please see the final page of this leaflet for Idaho Medicaid prior authorization criteria.**

The LA oral opioids morphine sulfate and oxycodone are routinely used in clinical practice and dosing and equipotent dose conversion guidelines are readily available. Methadone, on the other hand, is less commonly used and possesses important properties that clinicians must be aware of, including a variable (often long) half-life and extensive bioavailability, which make accumulation a concern following multiple doses. Furthermore, interpatient variability is even greater with methadone compared with other opioids and adds to the complexity of appropriately using this drug.⁴ **While clinicians should not be deterred from using methadone in their patients with CNMP, particular attention must be paid to its dynamic and kinetic intricacies. Experience from the Veteran’s Affairs (VA) medical system with methadone demonstrates the drug’s effectiveness and safety when used appropriately.**⁵ VA guidelines for the use of methadone in CNMP are included on page three of this leaflet.

Opioid Therapy for CNMP

The decision to begin long-term opioid therapy must be weighed carefully, especially in CNMP. Patients are candidates for opioids only if they have failed all other therapies. Although a history of past drug abuse may be considered a precaution for opioid use, most experts agree that appropriate analgesia should never be withheld, especially when routine follow up and monitoring can help avert potential problems.^{2,6} **LA opioid therapy, once stabilized, is associated with fewer adverse effects and better analgesia than as needed (PRN) short-acting opioids. Ideally, short-acting agents should only be used early in the treatment of CNMP while establishing an effective dose of a LA agent and then minimally thereafter for breakthrough pain.**⁶ In addition, it is recommended that the prescribing and dispensing of opioid therapy be carried out by one provider and one pharmacy for each patient.

General Dosing Recommendations

The World Health Organization (WHO) has published guidelines for the pharmacologic treatment of cancer pain and many of these strategies are useful in CNMP as well.⁷ It is important to note that there may be large interpatient variability in the equianalgesic

conversion ratio and a single ratio may not be applicable to all patients. Opioid dosing should be individualized and titrated slowly to response. **As a general rule, start low and go slow. If a patient develops marked sedation (which can be a precursor to respiratory depression), hold or decrease subsequent doses and/or lengthen the dosing interval. Reassess patients for adverse effects and efficacy (changes in pain scores and increased level of activity) once weekly during titration periods and once monthly after a stable daily dose has been reached.**^{5,6} The following table contains dosage and cost information for oral long-acting opioids. Fentanyl transdermal (Duragesic[®]) may also be used for CNMP, but is not an Idaho Medicaid preferred drug, requires additional explanation, and is not included in this review.

Equipotent Doses for Oral Long-Acting Opioids

Generic	Brand	Equi-analgesic Dose (mg)	Dosing interval	Cost**†
Morphine Sulfate	MS Contin [®]	30-40	Q 8-12 hrs	\$59.78 (30mg)
	Avinza ^{®*}		Q 24 hrs	\$81.30 (30 mg)
	Kadian ^{®*}		Q 12-24 hrs	\$67.78 (30 mg)
Oxycodone	Oxycontin [®]	15-30	Q 12 hrs	\$88.33 (20 mg) \$156.72 (40mg)
Levorphanol	Levo-Dromoran [®]	4	Q 8 hrs	\$64.34 (2mg) (60 tablets)
Methadone	Dolophine ^{®*}	10-20	Q 6-24 hrs	\$6.33 (10mg)
	Methadose [*]			\$4.23 (10mg)

*Idaho Medicaid Preferred Drugs

**Cost based on 30 tablets per Redbook 2004.

† Prices are not reflective of the acquisition costs for Idaho Medicaid.

Table adapted from MICROMEDEX[®] Narcotic Analgesic Comparative Review (cited 6/2004)

Patient Education

Patients should understand that initial doses of a LA agent may often be inadequate for pain relief. It is important to start low to avoid serious adverse effects such as respiratory depression. Patients should be encouraged to keep a pain medication diary, especially during the initiation and titration phases to help in achieving an appropriate dose.

Oftentimes patients may want to be maintained on shorter-acting opioids for “quick relief,” however, better outcomes and improved analgesia are associated with stabilized long-acting therapy with minimal breakthrough pain medication use.

Proper education on the place and rationale for long-acting agents should be reinforced.

Methadone Dosing

There has been no ideal dose titration schedule identified for opioid therapy. Several strategies have been developed by various organizations. For example, the VA medical system has considerable experience with methadone initiation and monitoring. A complete reference is available at: <http://www.vapbm.org/pbm/drugmonitoring.htm> Adaptations from the VA’s “Methadone Dosing Recommendations for Treatment of Chronic Pain” are included on the following page.

Dosing for Initiation of Methadone

Dosing Strategy	Initial Methadone Dose	Increments	Comments
Slow Titration	2.5mg q 8 hrs	↑ by 2.5mg q 8 hrs every 5 to 7 days	As a general rule, start low & go slow.
Rapid Titration	2.5mg q 6 to 8 hrs	↑ by 2.5mg q 6 to 8 hrs as often as every other day over ~4 days	

Dosing for patients previously receiving opioid therapy

Morphine-Equivalent Dose of Opioid (mg/day)	Calculated Methadone dose (mg/day)	Initial Methadone dose	Increment
<200	15mg	5mg q 8 hrs	↑ by 15mg every 5 to 7 days PRN
200-500	~7% of morphine equivalent	Calculated methadone dose given in divided doses q 8 hrs	↑ by 15mg every 5 to 7 days PRN
>500	~7% of morphine equivalent	1/3 of calculated methadone dose given in divided doses q 8 hrs (with 2/3 of previous opioid dose)	<ul style="list-style-type: none"> ▪ Add 1/3 of calculated methadone dose every 5 days. ▪ Decrease previous opioid by 1/3 every 5 days. ▪ Complete conversion period=15 days

References

- 1) Joranson DE, Ryan KM, Gilson AM, et al. Trends in medical use and abuse of opioid analgesics. JAMA 2000;283(13):1710-14.
- 2) The use of opioids for the treatment of chronic pain: a consensus statement from the American Academy of Pain Medicine and the American Pain Society. Glenview, Ill.: The American Academy of Pain Medicine and American Pain Society, 1997.
- 3) Evidence-Based Recommendation for Medical Management of Chronic Non-Malignant Pain, College of Physicians and Surgeons of Ontario, November 2000
- 4) Layson-Wolf C, Goode JV, Small RE. Clinical use of methadone. J Pain Palliat Care Pharmacother. 2002;16(1):29-59
- 5) Goodman F, Jones WN, Glassman P. Methadone Dosing Recommendations for Treatment of Chronic Pain. Available at: [http://www.vapbm.org/monitoring/Methadone%20Dosing%20Final%20\(Rcv%20081103\).pdf](http://www.vapbm.org/monitoring/Methadone%20Dosing%20Final%20(Rcv%20081103).pdf) (Cited 6/2004)
- 6) Ballantyne, JC, Mao, J. Opioid therapy for chronic pain. N Engl J Med 2003; 349:1943.
- 7) McCaffery M. Pain Control. Barriers to the use of available information. World Health Organization Expert Committee on Cancer Pain Relief and Active Supportive Care. Cancer. 1992 Sep 1:70 (Suppl):1438-39.

Idaho Medicaid LA Opioid Prior Authorization Criteria

Approval Criteria

- Prescriptions for any of the following preferred agents will be approved:
 - Kadian® (morphine sulfate extended release)
 - Avinza® (morphine sulfate extended release)
 - Methadone
 - Fentanyl, if patient is 65 years of age or older

- Non-preferred agents may be approved if the patient:
 - Has a history of one preferred agent in the last 6 months.
 - Malignant Pain (ICD-9 = 140-208, 99.25 or chemotherapy administration related CPT code)
 - Inability to swallow capsules or tablets
 - Allergy to morphine and/or methadone

Denial Criteria

- Non-preferred agents will be denied if the patient does not have a history of at least one preferred agent in the last 6 months.

