

## **Supplemental Material**

**1) Oregon High Dosage Policy**

**2) eTables**

**3) eFigures**

## Opioid Analgesics – High Dose

### Goal(s):

- Limit the use of high dose opioid therapy to above-the-line diagnoses that are supported by the medical literature
- Limit the use of non-preferred products
- Promote the safe use of opioids.
  - Opioids have been associated with an increasing proportion of deaths in Oregon and the US.
  - Opioid deaths in Oregon are often associated with concurrent use of other drugs (e.g. other opioids, benzodiazepines, skeletal muscle relaxants)
  - Opioid deaths in Oregon are often associated with patients with a history of drug abuse.
  - Buprenorphine, Fentanyl and Methadone carry FDA Black Box Warnings and have been associated with adverse cardiac effects associated with QTc prolongation and/or life-threatening hypoventilation.
    - This risk is increased with concurrent use of other drugs prolonging the QTc interval or other drugs affecting metabolism of methadone or fentanyl.
  - See Oregon DUR Board newsletter at:
    - [http://pharmacy.oregonstate.edu/drug\\_policy/pages/dur\\_board/newsletter/articles/volume11/DURV1112.pdf](http://pharmacy.oregonstate.edu/drug_policy/pages/dur_board/newsletter/articles/volume11/DURV1112.pdf)
    - [http://pharmacy.oregonstate.edu/drug\\_policy/pages/dur\\_board/newsletter/articles/volume5/DURV515.pdf](http://pharmacy.oregonstate.edu/drug_policy/pages/dur_board/newsletter/articles/volume5/DURV515.pdf)

### Initiative:

Long and Short Acting Opioid quantity and dose limits: preferred agents, approved indications, and dose limits.

### Length of Authorization:

**Up to 6 months**

### Covered Alternatives:

A list of preferred opioids is available at [http://www.oregon.gov/DHS/healthplan/tools\\_prov/pdl.shtml](http://www.oregon.gov/DHS/healthplan/tools_prov/pdl.shtml)

### Requires a PA:

- All non-preferred opioids and preferred opioids exceeding the dose threshold in the table below, not to exceed a Morphine Equivalent Dose (MED) of 120mg per day.
- Patient with terminal diagnosis, hospice, and metastatic neoplasm (ICD9 = 190xx – 199xx) are exempt from the PA requirements.

*-Approved Prior Authorizations may be subject to quantity limits*

| Dosing Threshold adapted from Washington State Agency Medical Directors Interagency Guideline on Opioid Dosing for Chronic Non-cancer Pain 2010 ( <a href="http://www.agencymeddirectors.wa.gov">www.agencymeddirectors.wa.gov</a> ) |                       |   |  |
|--|-----------------------|---|--|
| Opioid   | Dose threshold        | Recommended starting dose for opioid-naïve patients   | Considerations   |
| <b>Buprenorphine Transdermal</b>   | 20mcg/hour (q 7 days) | 5mcg/hr patch q 7 days  | May increase dose q72 hours patients up to a max of 20mcg/hr q 7 days. Doses >20mcg/hr q7days increase risk of QTc prolongation.   |
| <b>Fentanyl Transdermal</b>  | 50mcg/hour (q 72 hr)  | Use only in opioid-tolerant patients who have been taking ≥ 60mg MED daily for a week or longer |  |
| <b>Hydromorphone</b>   | 30mg per 24 hours     | 2mg q 4–6 hours   |  |
| <b>Methadone</b>   | 40mg per 24 hours     | 2.5-5mg BID – TID   | Methadone is difficult to titrate due to its half-life variability. It may take a long time to reach a stable level in the body. Methadone dose should not be increased more frequently than every 7 days. Do not use as PRN or combine with other long-acting (LA) opioids. |
| <b>Morphine</b>  | 120mg per 24 hours    | Immediate-release: 10mg q 4 hours   | Adjust dose for renal impairment.  |
|  |                       | Sustained-release: 15mg q 12 hours  |  |
| <b>Oxycodone</b>   | 80mg per 24 hours     | Immediate-release: 5mg q 4–6 hours  | See individual product labeling for maximum dosing of combination products. Avoid concurrent use of any OTC products containing acetaminophen (maximum dose = 4000mg/day x <10day or 2500mg/day for 10 days or more)   |
|  |                       | Sustained Release: 10mg q 12 hours  |  |
| <b>Oxymorphone</b>   | 40mg per 24 hours     | Immediate-release: 5–10mg q 4–6 hours   | <b>Use with extreme caution due to potential fatal interaction with alcohol or medications containing alcohol.</b>   |
|  |                       | Sustained Release: 10mg q 12 hours  |  |

| Dosing Threshold for select short acting opioids |                |  |
|--|----------------|--|
| Opioid   | Dose threshold | Considerations   |
| Codeine  | 800mg/day      |  |
| Hydrocodone                                      | 120mg/day      | Dosing limits based on combinations (e.g. acetaminophen, ibuprofen) may lower the maximum daily dose |

| Common indications OHP does not cover:*  | ICD9 Codes   |
|--|--|
| Disorders of soft tissue (including Fibromyalgia)  | 729.0-729.2,<br>729.31-729.39,<br>729.4-729.9,<br>V53.02   |
| Acute and chronic disorders of spine without one of the following neurologic impairments:<br>a. Reflex loss<br>b. Dermatomal muscle weakness<br>c. Dermatomal sensory loss<br>d. EMG or NCV evidence of nerve root impingement<br>e. Cauda equina syndrome<br>f. Neurogenic bowel or bladder | 721.0<br>721.2-721.3<br>721.7-721.8<br>721.90<br>722.0-722.6<br>722.8-722.9<br>723.1<br>723.5-723.9<br>724.1-724.2<br>724.5-724.9<br>739<br>839.2<br>847 |

\*Covered diagnoses are dependent on funding levels. A list of currently funded diagnoses can be found at [http://www.oregon.gov/OHA/OHPR/HSC/current\\_prior.shtml](http://www.oregon.gov/OHA/OHPR/HSC/current_prior.shtml)

| Approval Criteria   |   |  |
|---|---|--|
| 1. What is the patient's diagnosis?   | Record ICD9   |  |
| 2. Is the request for methadone >100mg?   | Yes: Go to 3  | No: Go to 5  |
| 3. Does the patient have any of the following QTc Risk Factors?<br><ul style="list-style-type: none"> <li>Family history of "long QTc syndrome", syncope, sudden death</li> <li>Potassium depletion primary or secondary to drug use ( i.e. diuretics)</li> <li>Concurrent use of C34 inhibitors or QTc prolonging drugs (see table below)</li> <li>Structural heart disease, arrhythmias, syncope</li> </ul> | Yes: Go to 4  | No: Go to 5  |
| 4. Is this new therapy (i.e. no previous prescription for the same drug last month)?  | Yes: Pass to RPH; Deny, (Medical Appropriateness)<br>Go over black box warning and offer alternatives (e.g. Fentanyl transdermal, morphine extended release). | No: Pass to RPH, Approve for 30-60 days to allow time to taper or transition to alternative. Direct to DUR Newsletter for assistance. Refer to Rx "Lock-in" Program for evaluation and monitoring. |

|   |  |   |
|---|--|---|
| 5. Is the patient being treated for any of the following:<br>a. Oncology pain (ICD-9 338.3)<br>b. Terminal diagnosis (<6 months)<br>c. Hospice care | <b>Yes:</b> Go to #6   | <b>No:</b> Go to #8   |
| 6. Is the requested medication a preferred agent?   | <b>Yes:</b> Approve for up to 6 months   | <b>No:</b> Go to #7   |
| 7. Will the prescriber consider a change to a preferred product?  | <b>Yes:</b> Inform provider of covered alternatives in class.  | <b>No:</b> Approve for up to 6 months   |
| 8. Will the prescriber consider a change to a preferred product not to exceed 120mg MED?  | <b>Yes:</b> Inform provider of covered alternatives in class.  | <b>No:</b> Go to #9   |
| 9. Is the diagnosis covered by the OHP?   | <b>Yes:</b> Go to #10  | <b>No:</b> Pass to RPh, Deny (Not Covered by the OHP)<br><br>May approve for 30-60 days to allow for tapering   |
| 10. Is this new therapy (i.e. no previous prescription for the same drug, same dose last month)?  | <b>Yes:</b> Go to #11  | <b>No:</b> Go To #12  |
| 11. Does the total daily opioid dose exceed 120mg MED?  | <b>Yes: Pass to RPh, Deny (Medical Appropriateness)</b><br><br>In general, the total dose of opioid should not exceed 120mg MED Risks substantially increase at doses at or above 100mg MED.<br><br>Alternatives:<br>Preferred NSAIDs or LAOs @ doses < 120mg MED. | <b>No:</b> Go to #12  |
| 12. Has the patient had a recent urinary drug screen (within the past 90 days)?   | <b>Yes:</b> Go to #13  | <b>No:</b> Pass to RPH: Deny (Medical Appropriateness)<br><br>Recommend Urine Drug Screen   |
| 13. Is the patient seeing a single prescribing practice & pharmacy for pain treatment (short and long acting opioids)?                              | <b>Yes:</b> Go To #14  | <b>No:</b> <u>Approve 30-90 days;</u><br><br>Refer to Rx Lock-In program for evaluation.<br><br>Further approvals pending RetroDUR / Medical Director review of case. |
| 14. Does the total daily opioid dose exceed 120mg MED?  | <b>Yes:</b> Go to #15  | <b>No:</b> Go to #16  |

|   |  |   |
|---|--|---|
| <p>15. Can the prescriber provide documentation of sustained improvement in both function and pain AND is prescriber is aware of additional risk factors (e.g. concurrent benzodiazepines, skeletal muscle relaxants, other LAO or history of drug abuse)?</p>  | <p><b>Yes: Approve up to 6 months.</b></p> <p><b>Quantity Limits Apply, e.g.:</b><br/> Avinza: 1 dose / day<br/> Butrans: 1 patch / week<br/> Embeda: 2 doses / day<br/> Exalgo: 1 dose / day<br/> Fentanyl: 1 patch / 72 hours<br/> Kadian: 2 doses / day<br/> Opana XR: 2 doses / day<br/> Oxycodone ER: 2 doses / day</p> | <p><b>No: Approve 30-90 days to allow for potential tapering of dose.</b></p> <p>Refer to Rx Lock-In program for evaluation.</p> <p>Further approvals pending RetroDUR / Medical Director review of case.</p>             |
| <p>16. Is the patient concurrently on other long-acting opioids (e.g. fentanyl patches, methadone, or long-acting morphine, long-acting oxycodone, and long-acting oxymorphone)?</p>  | <p><b>Yes: Go to #17</b></p>   | <p><b>No: Approve for up to 6 months</b></p>  |
| <p>17. Is the duplication due to tapering or switching products?</p> <p>The concurrent use of multiple long-acting opioids is not recommended unless tapering and switching products. Consider a higher daily dose of a single long-acting opioid combined with an immediate release product for breakthrough pain.</p> | <p><b>Yes: Approve for 30-90 days</b> at which time duplication LAO therapy will no longer be approved.</p>  | <p><b>No: Deny</b> (Medical Appropriateness)</p> <p><b>May approve for taper only.</b></p> <p>Refer to Rx Lock-In program for evaluation.</p> <p>If necessary, inform prescriber of provider reconsideration process.</p> |

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*P&T or DUR Board Action:* 2/23/12 (TDW), 11/17/11(KK); 12/3/09 (KS), 9/9/09(klk), 12/4/08klk, 3/19/09  
*Revision(s):* 6/21/12, 5/14/12; 1/1/12; 1/1/10  
*Initiated:* 7/1/09

**eTable 1: Morphine equivalent dose conversions.**

| Opioid                               | Conversion Factor |
|--------------------------------------|-------------------|
| CODEINE PHOSPHATE                    | 0.15              |
| BUPRENORPHINE                        | 12.6              |
| BUTORPHANOL TARTRATE                 | 7                 |
| DIHYDROCODEINE                       | 0.25              |
| FENTANYL TRANSDERMAL                 | 7.2               |
| FENTANYL CITRATE TABLET EFF, LOZENGE | 0.13              |
| FENTANYL CITRATE SPRAY               | 0.16              |
| FENTANYL CITRATE FILM                | 0.18              |
| HYDROCODONE                          | 1                 |
| HYDROMORPHONE HCL                    | 4                 |
| LEVOMETHADYL ACETATE HCL             | 8                 |
| LEVORPHANOL TARTRATE                 | 11                |
| MEPERIDINE HCL                       | 0.1               |
| METHADONE HCL                        | 3                 |
| MORPHINE SULFATE                     | 1                 |
| NALBUPHINE HCL                       | 1                 |
| OPIUM TINCTURE                       | 1                 |
| OXYCODONE HCL                        | 1.5               |
| OXYMORPHONE HCL                      | 3                 |
| PENTAZOCINE LACTATE                  | 0.37              |
| PROPOXYPHENE HCL                     | 0.23              |
| TAPENTADOL HCL                       | 0.4               |
| TRAMADOL HCL                         | 0.1               |

**Sources:**

Conversion data were provided to investigators by US Centers for Disease Control

Von Korff M, Saunders K, Ray GT, Boudreau D, Campbell C, Merrill J, et al. De Facto Long-term Opioid Therapy for Noncancer Pain. The Clinical Journal of Pain 2008;24:521-527.

Technical Assistance Guide No. 01-13: Calculating Daily Morphine Milligram Equivalents. Waltham (MA): Prescription Drug Monitoring Program Technical Assistance Center; 2013.

[http://www.pdmpassist.org/pdf/BJA\\_performance\\_measure\\_aid\\_MME\\_conversion.pdf](http://www.pdmpassist.org/pdf/BJA_performance_measure_aid_MME_conversion.pdf).

**eTable 2: Non-opioid medications**

|                                   |
|-----------------------------------|
| <b>Benzodiazepines</b>            |
| ALPRAZOLAM                        |
| ALPRAZOLAM/DIETARY SUPPL NO.17    |
| CHLORDIAZEPOXIDE                  |
| CHLORDIAZEPOXIDE HCL              |
| CHLORDIAZEPOXIDE/METHYLSCOPOLA    |
| CLORAZEPATE DIPOTASSIUM           |
| DIAZEPAM                          |
| DIAZEPAM/SOYBEAN OIL              |
| ESTAZOLAM                         |
| FLURAZEPAM HCL                    |
| HALAZEPAM                         |
| LORAZEPAM                         |
| LORAZEPAM/0.9% SODIUM CHLORIDE    |
| LORAZEPAM/D5W                     |
| MIDAZOLAM                         |
| MIDAZOLAM HCL                     |
| MIDAZOLAM HCL IN 0.9 % NAACL      |
| MIDAZOLAM HCL IN 0.9 % NAACL/PF   |
| MIDAZOLAM HCL/PF                  |
| MIDAZOLAM IN D5W                  |
| MIDAZOLAM IN D5W/PF               |
| OXAZEPAM                          |
| QUAZEPAM                          |
| TEMAZEPAM                         |
| TEMAZEPAM/DIET8                   |
| TRIAZOLAM                         |
| <b>Drugs for neuropathic pain</b> |
| ACYCLOVIR/LIDOCAINE HCL           |
| AMITRIPTYLINE HCL                 |
| BACITRACIN/LIDOCAINE              |
| BUPIVACAINE HCL/LIDOCAINE HCL     |
| CARBAMAZEPINE                     |
| CEFTRIAZONE SOD/LIDOCAINE HCL     |
| DESIPRAMINE HCL                   |
| DESVENLAFAXINE                    |
| DESVENLAFAXINE FUMARATE           |
| DESVENLAFAXINE SUCCINATE          |
| DEXAMETH PH/LIDOCAINE HCL         |
| DIVALPROEX SODIUM                 |
| DOXEPIN HCL                       |
| DULOXETINE HCL                    |

|                                |
|--------------------------------|
| FOSPHENYTOIN SODIUM            |
| GABAPENTIN                     |
| GABAPENTIN ENACARBIL           |
| GABAPENTIN/DIETARY SUPPL NO.11 |
| HYDROCORT/LIDOCAINE IN COLEUS  |
| HYDROCORTISONE AC/LIDOCAINE    |
| HYDROCORTISONE/LIDOCAINE/ALOE  |
| HYDROCORTISONE/LIDOCAINE/CLNS6 |
| IMIPRAMINE HCL                 |
| IMIPRAMINE PAMOATE             |
| LACOSAMIDE                     |
| LAMOTRIGINE                    |
| LEUPROLIDE/LIDOCAINE HCL       |
| LEVETIRACETAM                  |
| LEVETIRACETAM IN NACL (ISO-OS) |
| LEVOMILNACIPRAN HYDROCHLORIDE  |
| LIDOCAINE                      |
| LIDOCAINE HCL                  |
| LIDOCAINE HCL IN 0.9 % NACL/PF |
| LIDOCAINE HCL/BENZALK CHL      |
| LIDOCAINE HCL/BENZALK CHL/ALC  |
| LIDOCAINE HCL/BENZETHONIUM CL  |
| LIDOCAINE HCL/CAPSAICIN        |
| LIDOCAINE HCL/COLLAGEN         |
| LIDOCAINE HCL/D5W              |
| LIDOCAINE HCL/D5W/PF           |
| LIDOCAINE HCL/D7.5W/PF         |
| LIDOCAINE HCL/EPINEPHRINE      |
| LIDOCAINE HCL/EPINEPHRINE BIT  |
| LIDOCAINE HCL/EPINEPHRINE/PF   |
| LIDOCAINE HCL/GLUCOSE          |
| LIDOCAINE HCL/GLYCERIN         |
| LIDOCAINE HCL/MENTHOL          |
| LIDOCAINE HCL/PF               |
| LIDOCAINE HCL/VIT E/TEA TREE   |
| LIDOCAINE WITH 8.4% SOD BICARB |
| LIDOCAINE/ALLANTOIN/PETROLATUM |
| LIDOCAINE/ALOE VERA            |
| LIDOCAINE/BENZALK CHL          |
| LIDOCAINE/BENZALKONIUM CL/IPA  |
| LIDOCAINE/BENZETHON CL         |
| LIDOCAINE/CAPSAICIN/MENTHOL    |
| LIDOCAINE/CHLOROXYLENOL/PHENOL |
| LIDOCAINE/COLLAGEN,BOVINE      |



|                                |
|--------------------------------|
| LIDOCAINE/DEXTROSE-WATER       |
| LIDOCAINE/EPINEPHR/TETRACAINE  |
| LIDOCAINE/HYALUR AC/ALOE/COLL  |
| LIDOCAINE/HYDROCORT/PSYLLIUM   |
| LIDOCAINE/MENTHOL              |
| LIDOCAINE/MENTHOL/ALOE VERA    |
| LIDOCAINE/METHYL SAL/MENTHOL   |
| LIDOCAINE/PHENOL LIQUID        |
| LIDOCAINE/POVIDONE-IODINE      |
| LIDOCAINE/PRILOCAINE           |
| LIDOCAINE/TETRACAINE           |
| LIDOCAINE/TRANSPARENT DRESSING |
| MAG&AL/SIM/DIPHENHYD/LIDOCAINE |
| MEPHENYTOIN                    |
| MILNACIPRAN HCL                |
| NORTRIPTYLINE HCL              |
| NYSTATIN/LIDOCAINE/DIPHENHYD   |
| OXCARBAZEPINE                  |
| OXYTETRACYCLINE/LIDOCAINE      |
| PERPHENAZINE/AMITRIPTYLINE HCL |
| PHENTERMINE/TOPIRAMATE         |
| PHENYTOIN                      |
| PHENYTOIN SODIUM               |
| PHENYTOIN SODIUM EXTENDED      |
| PREGABALIN                     |
| PROTRIPTYLINE HCL              |
| TOPIRAMATE                     |
| TRIAMCINOLONE/LIDOCAINE        |
| TRIMIPRAMINE MALEATE           |
| VALPROIC ACID                  |
| VALPROIC ACID (AS SODIUM SALT) |
| VENLAFAXINE HCL                |
| <b>Drugs for arthritis</b>     |
| ABATACEPT                      |
| ABATACEPT/MALTOSE              |
| ADALIMUMAB                     |
| ALLOPURINOL                    |
| ALLOPURINOL SODIUM             |
| ANAKINRA                       |
| ANTIARTHRITIC COMBINATION NO.2 |
| APREMILAST                     |
| AURANOFIN                      |
| AUROTHIOGLUCOSE                |
| CELECOXIB                      |

|                                |
|--------------------------------|
| COLCHICINE                     |
| COLCHICINE/PROBENECID          |
| COLCHICINE/RHUS EXTRACTS       |
| DICLOFENAC EPOLAMINE           |
| DICLOFENAC SODIUM              |
| DICLOFENAC SODIUM/MISOPROSTOL  |
| DICLOFENAC SUBMICRONIZED       |
| ETANERCEPT                     |
| ETODOLAC                       |
| FEBUXOSTAT                     |
| FENOPROFEN CALCIUM             |
| FLURBIPROFEN                   |
| GLU/CHON-MSM#1/D3/C/MN/BOS/BOR |
| GLUC 2KCL/CHONDR/COLL HY/HY AC |
| GLUC HCL/CHON SU/MV/FA/KUD ISO |
| GLUC HCL/CHON/MV/MIN AA/HB 162 |
| GLUC HCL/CSA/COLL HY/HYALUR AC |
| GLUC HCL/CSANA/GLY-AM-GLY,MX   |
| GLUC HCL/CSANA/GLY-AM-GLY,MX/C |
| GLUC HCL/GLUC SU/AC-ALP-D-GLUC |
| GLUC HCL/MSM/C/MN/WILLOW/GING  |
| GLUC SU 2KCL/CHONDR/VIT C/MANG |
| GLUC SU 2KCL/CHONDRO SU A/C/MN |
| GLUC SU 2KCL/MSM/CSA/CAL/HC115 |
| GLUC SU DIPO CH/CHON SU/C/MANG |
| GLUC SU/CHONDR SU A NA/SODIUM  |
| GLUC SU/CHONDR SU A NA/VIT C   |
| GLUC SU/CHONDRO SU A/VIT C/MN  |
| GLUC SU/FE/SOD/VIT C/VITAMIN E |
| GLUC SU/MSM/CHONDRO SU A/C/MN  |
| GLUC SU/MSM/MAGNESIUM/VIT C    |
| GLUC SU/OMEGA-3/VITAMIN E      |
| GLUC/CHND/OM3/DHA/EPA/FISH/STR |
| GLUC/CHON-MSM#1/C/MANG/BOS/BOR |
| GLUC/CHON-MSM#1/VIT C/MANG/BOR |
| GLUC/CHON-MSM#2/C/D3/MANG/BORN |
| GLUC/CHON-MSM#3/MANG/BOSW/BOR  |
| GLUC/MSM/COLL2/HYAL/ANTIARTH#3 |
| GLUCOS/MSM/COLG II/C/MAN/HRB21 |
| GLUCOSA SU 2KCL/CHONDROITIN SU |
| GLUCOSAM & CHONDROIT-MV & MIN3 |
| GLUCOSAM HCL/CHONDRO SU A/C    |
| GLUCOSAM HCL/CHONDRO SU A/C/MN |
| GLUCOSAM HCL/VIT C/ZN/CU/MANG  |

|                                |
|--------------------------------|
| GLUCOSAM SU/CHONDROITIN/AO MV5 |
| GLUCOSAM SUL NA/CHONDR SU A NA |
| GLUCOSAM-CHONDRO-HERB 149-HYAL |
| GLUCOSAM/CHON-COL.CPLX/D3/C/MN |
| GLUCOSAM/CHONDROIT/C/MANGANESE |
| GLUCOSAM/CHONDROITIN/DIET CB13 |
| GLUCOSAM/CHONDROITIN/DIET CB25 |
| GLUCOSAM/MSM/CHOND/BOSW/HYALUR |
| GLUCOSAM/MSM/CHOND/HRB149/HYAL |
| GLUCOSAM/MSM/CHOND/HYALURON AC |
| GLUCOSAM/MSM/CHONDR/VIT C/HYAL |
| GLUCOSAM/MSM/CHONDROIT/VIT D3  |
| GLUCOSAM/MSM/VIT C/MANG/HRB#21 |
| GLUCOSAMINE HCL                |
| GLUCOSAMINE HCL AND SULFATE    |
| GLUCOSAMINE HCL/CHONDR SU A NA |
| GLUCOSAMINE HCL/MSM            |
| GLUCOSAMINE HCL/S-ADENOSYLMET  |
| GLUCOSAMINE HCL/VITAMIN D3     |
| GLUCOSAMINE SULF/CHONDROITIN A |
| GLUCOSAMINE SULFATE            |
| GLUCOSAMINE SULFATE 2KCL       |
| GLUCOSAMINE SULFATE 2KCL/MSM   |
| GLUCOSAMINE SULFATE SODIUM CL  |
| GLUCOSAMINE SULFATE/MSM        |
| GLUCOSAMINE/CHONDRO SU A       |
| GLUCOSAMINE/CHONDROIT/CAL/PHEL |
| GLUCOSAMINE/CHONDROITIN A/MSM  |
| GLUCOSAMINE/CHONDROITIN SULF A |
| GLUCOSAMINE/CHONDROITIN/VIT D3 |
| GLUCOSAMINE/CHONDROITN/NA/C/SE |
| GLUCOSAMINE/CONDROITIN/HRB#182 |
| GLUCOSAMINE/D3/BOSWELLIA SERRA |
| GLUCOSAMINE/MSM/CHONDROIT SULF |
| GLUCOSAMINE/MSM/CHONDROITIN A  |
| GLUCOSAMN/CONDROITN/C/MN/BORON |
| GOLD SODIUM THIOMALATE         |
| GOLIMUMAB                      |
| HYALURONATE SOD, CROSS-LINKED  |
| HYALURONATE SODIUM             |
| HYALURONATE SODIUM, STABILIZED |
| HYLAN G-F 20                   |
| IBUPROFEN                      |
| IBUPROFEN/CAFF/B1/B2/B6/B12    |

|                                |
|--------------------------------|
| IBUPROFEN/DIET. SUPP 11        |
| IBUPROFEN/FAMOTIDINE           |
| IBUPROFEN/IRR CNT-IRRIT CMB #2 |
| INDOMETHACIN                   |
| KETOPROFEN                     |
| LANSOPRAZOLE/NAPROXEN          |
| LEFLUNOMIDE                    |
| MECLOFENAMATE SODIUM           |
| MELOXICAM                      |
| MELOXICAM/IRR CNTR-IRR CMB #2  |
| METHOTREXATE SODIUM            |
| METHOTREXATE/PF                |
| NABUMETONE                     |
| NAPROXEN                       |
| NAPROXEN SODIUM                |
| NAPROXEN/DIET. SUPP 11         |
| NAPROXEN/ESOMEPRAZOLE MAG      |
| NAPROXEN/IRR CNTR-IRRIT CMB #2 |
| OXAPROZIN                      |
| PEGLOTICASE                    |
| PENICILLAMINE                  |
| PIROXICAM                      |
| PIROXICAM/DIET. SUPP 11        |
| PROBENECID                     |
| RASBURICASE                    |
| ROFECOXIB                      |
| SALSALATE                      |
| SULFINPYRAZONE                 |
| SULINDAC                       |
| TOFACITINIB CITRATE            |
| TOLMETIN SODIUM                |
| VALDECOXIB                     |

**eTable 3: ICD9 Diagnosis Codes**

| Category  | ICD-9   |
|---|---|
| <b>Gagne Measures (alcohol diagnosis omitted because of substance use disorder data suppression in Colorado data)</b> |   |
| Anemia  | >= '2801' AND <= '2819'   |
|   | Like '2859*'  |
| Arrhythmia  | IN ('42610','42611','42613','42731','42760')  |
|   | >= '4262' AND <= '4264'   |
|   | >= '42650' AND <= '42653'   |
|   | >= '4266' AND <= '4268'   |
|   | Like '4270*' Or Like '4272*' Or Like '4279*' Or Like '7850*' Or Like 'V450*' Or Like 'V533*'                            |
| CHF   | IN ('40201','40211','40291') Or Like '4293*' Or Like '425*' Or Like '428*'  |
| Coagulopathy  | >= '2860' AND <= '2869'   |
|   | >= '2873' AND <= '2875'   |
|   | Like '2871*'  |
| Comp Diabetes   | >= '25040' AND <= '25073'   |
|   | >= '25090' AND <= '25093'   |
| Dementia  | Like '3310*' Or Like '3311*' Or Like '3312*' Or Like '290*'   |
| Electrolytes  | >= '2760' AND <= '2769'   |
| Hemiplegia  | Like '342*' Or Like '344*'  |
| HIV/Aids  | Like '042*' Or Like '043*' Or Like '044*'   |
| Hypertension  | Like '4011*' Or Like '4019*'  |
|   | IN ('40210','40290','40410','40490','40511','40519','40591','40599')  |
| Liver   | IN ('07032','07033','07054','45620','45621')  |
|   | >= '57140' AND <= '57149'   |
|   | Like '4560*' Or Like '4561*' Or Like '5710*' Or Like '5712*' Or Like '5713*' Or Like '5715*' Or Like '5716*'            |
|   | Like '5718*' Or Like '5719*' Or Like '5723*' Or Like '5728*' Or Like 'V427*'  |
| Metastatic  | Like '196*' Or Like '197*' Or Like '198*' Or Like '199*'  |
| Psychosis   | >= '29500' AND <= '29899'   |
|   | IN ('29910','29911')  |
| Pulmonary circulation disorders   | Like '416*' Or Like '4179*'   |
|   | Like '4150*' Or Like '4168*' Or Like '4169*' Or Like '491*' Or Like '492*' Or Like '493*' Or Like '494*' Or Like '496*' |
| PVD   | >= '4400' AND <= '4409'   |
|   | >= '4431' AND <= '4439'   |
|   | Like '4412*' Or Like '4414*' Or Like '4417*' Or Like '4419*'  |
|   | Like '4471*' Or Like '5571*' Or Like '5579*' Or Like 'V434*'  |
| Renal   | IN ('40311','40391','40412','40492')  |
|   | Like '585*' Or Like '586*' Or Like 'V420*' Or Like 'V451*' Or Like 'V560*' Or Like 'V568*'                              |
| Tumor   | >= '140' AND <= '171'   |
|   | >= '174' AND <= '195'   |
|   | Like '2730*' Or Like '2733*' Or Like 'V1046*'   |
|   | >= '200' AND <= '208'   |

|                                |  |
|--------------------------------|--|
| Weight Loss                    | Like '260*' Or Like '261*' Or Like '262*' Or Like '263*'   |
| <b>Mental Health Diagnoses</b> |  |
| ADHD                           | Like '314*'  |
| Adjustment Disorder            | Like '3090*' Or Like '3092*'   |
| Anxiety Disorder               | >= '300' and < '3004'  |
| Anxiety Disorder               | >= '3005' and < '301'  |
| Bipolar                        | Like '2960*' Or Like '2961*' Or Like '2964*' Or Like '2965*' Or Like '2966*' Or Like '2967*'   |
| Bipolar                        | IN ('29689','30111')   |
| Dementia                       | Like '290*' Or Like '3310*' Or Like '3312*' Or Like '3318*'  |
| Depression                     | Like '2962*' Or Like '2963*' Or Like '2980*' Or Like '3004*' Or Like '3091*' Or Like '311*'  |
| PTSD                           | = '30981'  |
| Schizophrenia                  | Like '295*'  |
| <b>Acute pain</b>              |  |
| Sickle cell with crisis        | 282.62   |
| Acute pain                     | Like '338.11*' Or Like '33812*' Or Like '33818*' Or Like '33819*'  |
| Dental ab scess with sinus     | = '5225'   |
| Dental abscess without sinus   | = '5227'   |
| Gallstone                      | Like '574*'  |
| Acute pancreatitis             | Like '577*'  |
| Kidney stone                   | Like '592*'  |
| Pathologic fracture            | Like '7331*'   |
| Acute injury                   | >= Like '800*' and <= '904.9*'   |
| Other acute injury             | >= Like '910*' and <= Like '9599*'   |
| External cause of injury codes | >= Like 'E800*' and <='E8499*' Or >= Like 'E880*' and <='E9099*' Or >= Like 'E916*' and <='E9289*' Or >= Like 'E953*' and <='E9689*' Or >= Like 'E970*' and <='E9769*' Or >= Like 'E983*' and <='E9999*' |

## eFigure Descriptions

**eFigure 2:** Other medication fills per 100 enrolled individuals from January 2011 to December 2013 in Oregon and Colorado. Solid line indicates Oregon, and dashed line indicates Colorado; Vertical lines indicate policy implementation period April 2012 to June 2012. \* $p < 0.0001$  \*\* $p < 0.001$  \*\*\* $p < 0.05$

**eFigure 3:** Opioid overlap with other opioids, benzodiazepines, and non-benzodiazepine sedative hypnotics per 100 enrolled individuals from January 2011 to December 2013 in Oregon and Colorado. Solid line indicates Oregon, and dashed line indicates Colorado; Vertical lines indicate policy implementation period April 2012 to June 2012. \* $p < 0.0001$  \*\* $p < 0.001$  \*\*\* $p < 0.05$

**eFigure 4:** Other high risk opioid indicators per 100 enrolled individuals from January 2011 to December 2013 in Oregon and Colorado. Solid line indicates Oregon, and dashed line indicates Colorado; Vertical lines indicate policy implementation period April 2012 to June 2012. LAO is long-acting opioid. \* $p < 0.0001$  \*\* $p < 0.001$  \*\*\* $p < 0.05$

**eFigure 5:** Opioid-related emergency department (ED) visits, hospitalizations, or combined outcome per 100 enrolled individuals from January 2011 to December 2013 in Oregon and Colorado. Solid line indicates Oregon, and dashed line indicates Colorado; Vertical lines indicate policy implementation period April 2012 to June 2012. \* $p < 0.0001$  \*\* $p < 0.001$  \*\*\* $p < 0.05$









