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1515 Oak Street  
Eugene, Oregon 97401



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1515 OAK STREET  
EUGENE, OREGON 97401

**Pharmacists:**

**Kate James, R.Ph.**  
**Sheri Cannell, R.Ph.**  
**Heather Wilson, R.Ph.**

**Tel: 541-684-9352**  
**Fax: 541-684-0858**

[www.broadwayapothecary.com](http://www.broadwayapothecary.com)  
[broadway@broadwayapothecary.com](mailto:broadway@broadwayapothecary.com)

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## Dosing, Dosing Conversions, and Dosage Forms Using Opioids for Pain Management

Lloyd V. Allen, Jr., PhD, RPh  
Editor-in-Chief  
International Journal of Pharmaceutical Compounding

Pain is one of the most important responses of the body, as it serves as an “alerting” mechanism that something may be wrong. It is said to be the second most common chief presenting complaint by patients to primary care physicians, accounts for about 25% of all sick time lost from work, and statistics show that about 30 million people in the U.S. suffer from severe pain at least monthly.<sup>1</sup>

Medical research is making great strides in the diagnosis of pain and in determining its sources, mechanisms, and the body’s responses. As well as different approaches to minimize and prevent pain, a number of modalities are available to treat pain, to include:

- Biopsychosocial
- Chemical
- Dietary
- Pharmacological
- Physical
- Psychological

The result of pain includes a decrease in the patient’s quality of life, prevention from achieving one’s life goals, exorbitant healthcare costs, lost work, and general human suffering. There are numerous aspects of pain that must be considered overall, including classification, types, causes, sources, associated pathology, prognosis, treatment, social and environmental effects, economics, outcomes, prevention, and pathophysiology.

### FOCUS OF THIS PAPER

The focus of this paper will be on treatment methods involving dosing, dosing conversions, and dosage forms for the pharmacological treatment of pain.

When prescribing compounded pain management preparations, the physician has a great deal of flexibility in the quantity of drug to be used, unlike the commercial products that come only in certain strengths. Not only that, but most commercial products are only provided in oral or parenteral dosage forms with very few patches available. **Oral** compounded formulations may include, among others:

- Capsules
- Gummy bears
- Liquids
- Lollipops
- Lozenges

**Parenteral** dosage forms can include those for all different routes of administration and can be prepared in different dosage strengths and even in combinations; many of these may be suitable for **intrathecal pump administration**, etc. **Transdermal gels** are applied topically and utilize penetration enhancing agents to enable higher rates of penetration and better compliance with the patient since they are easy to administer. **Suppositories** and **oral inhalation** solutions are also options. (See the accompanying sidebar for prescribing options.)

### DOSING IN PAIN

Dosing of analgesics for patients should be sufficient just to obtain the level of relief desired by the patient and physician. It has been said that generally there is no need for anyone to suffer pain; there is a wide variety of analgesics available that can be used at different dosage strengths and many different delivery systems (dosage forms) that can be selected.

Generally, there is no advantage to parenteral administration over equianalgesic doses of orally administered medications. If oral dosing is not feasible, **sublingual/buccal**, **oral inhalation**, and **transdermal** are alternative noninvasive routes that can be considered before using parenteral administration.

When using morphine, it is best done with the immediate-release tablets. Once the dose has been titrated, then a slow-release formulation can be used. Dosing is usually best done on a regular schedule around-the-clock using “as needed” doses for breakthrough pain.

Table 1 contains different analgesics. These analgesics are arranged by categories, to include their usual dosages and a usual 24-hour dosage range that can be considered. Table 2 contains a comparison of narcotics, their dosages, and equivalencies to morphine, a universal standard for narcotics.

# NARCOTIC ANALGESICS

Some general guidelines for often-used narcotic analgesics include the following<sup>2,3</sup>:

1. Morphine 10 mg subcutaneous can often be used as a starting dose for acute severe pain in normal, narcotic-naïve, middle-aged, 70-kg patients. Older and younger patients, and patients with metabolic problems or liver disease, should have small initial dosages.
2. The relative potency of intramuscular:oral (PO) morphine of 1:6 changes to a 1:2-3 with chronic dosing. Based on acute, short-term use, chronic administration possibly alters the pharmacokinetics of the drug, and the morphine PO:parenteral ratio decreases to about 1.5-2.5:1.
3. Individualization of dosage is required for every patient.
4. Since meperidine (Demerol) is metabolized to nor-meperidine, which can cause seizure disorders and accumulates over time, a different opiate may be indicated.
5. Fentanyl patch (Duragesic) does not reach its full onset of action for several hours after attachment to the skin. The drug's effect will continue after removal from the skin due to the reservoir of drug in the skin that will continue to be absorbed.
6. Dosing fentanyl can be done as follows: If the amount of morphine or "morphine equivalents" given the last 24 hours is less than 134 mg, use 25 mcg/hour; if 135 to 214 mg, use 50 mcg/hr; if 225 to 314 mg, use 75 mcg/hour, etc.
7. Since codeine may produce excitation and constipation, a dose of 15 to 30 mg with a nonsteroidal anti-inflammatory drug or acetaminophen for an additive effect is often used.
8. Careful patient monitoring is required as the patient goes from acute to chronic dosing.

Converting from one opioid to another would seem to be a rather simple process, at least theoretically; find the right ratio/correlation, do the math, and there it is. However, experts disagree on what the appropriate ratios/correlations are. Studies continually challenge the conversion ratios. Historically, some of these ratios have been based on single-dose comparisons (acute) rather than on chronic dosing. The final conversion depends upon numerous factors, including dosage, tolerance, cross-tolerance, physiologic variations in metabolism, etc. Also to be considered include residual narcotics in the patient's system and the time required to achieve steady-state blood levels with the new drug while the former drug is being metabolized and excreted.

The tables and comments provided should be reviewed together and in context with a specific patient's needs; they are only a guide, and the final decision rests with the physician.

## REFERENCES

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## CONVERSION METHOD:

1. Determine the 24-hour equivalent of the **current drug**.
2. Obtain the conversion equivalent for the **new drug**.
3. Calculate the 24-hour equivalent of the **new drug** using the conversion equivalent.
4. Determine the desired dosing interval for the **new drug** based on the dosage form.
5. Divide the 24 hours by the new dosing interval to get the number of doses per 24-hour period (e.g., 24 hours/6 hours for a 6-hour interval yields 4 doses in 24 hours).
6. Divide the 24-hour dose by the number of doses in 24 hours to get the dose for each dosing interval.
7. Round off as needed and appropriate.
8. Consider any residual drug in the patient's system remaining from long-acting opioids or fentanyl patches, etc.
9. This can be a reasonable starting dose.
10. The dose and dosing interval can be changed based upon the responses of the patient.

In summary, this can be stated as:

$$\text{New 24-hr dose} = \frac{\text{Current 24-hr dose} \times (\text{New 24-hr Equivalent Drug Dose})}{(\text{Current 24-hr Equivalent Drug Dose})}$$

It should be remembered that simplistic equations and conversions do not replace patient observation and response and practitioner judgment.

### Notes:

1. Codeine: Actual potency is quite variable and codeine is metabolized into morphine (however, about 10% of the population has difficulty doing this and some drugs may inhibit this).
2. Fentanyl: Fentanyl patches are available ranging from 25 to 100 microgram per hour and are changed every 72 hours. A 25-mcg/h patch is approximately equivalent to 50 to 75 mg or oral morphine over 24 hours. The manufacturer of the patch does not present a simple conversion but suggests a conservative dosing schedule. They suggest a higher patch strength at lower morphine doses and a lower patch strength at higher morphine doses.
3. Hydrocodone: Most conversion tables do not list a conversion value. Some recommend the conversion factor for oxycodone as a starting point since they are very similar in potency.
4. Hydromorphone: There is still controversy regarding the potency ratio of hydromorphone compared to morphine. Earlier, it was thought there was a 7:1 hydromorphone:morphine ratio, but recently 5:1 relative potency is described.
5. Methadone: There also is considerable controversy here. Generally, some suggest using low equivalent doses of methadone initially, gradually increasing the dose, using more liberal doses for breakthrough pain during the conversion process.
6. Oxycodone: Conversion values differ here and suggests that oxycodone is about 1.5 to 2 times as strong as morphine.

**TABLE 1. DRUG EQUIVALENCES OF SELECTED OPIOIDS.<sup>2</sup>**

| DRUG NAME             | ROUTE OF ADMINISTRATION | 24-HOUR EQUIVALENT                    | DOSING EQUIVALENT |
|-----------------------|-------------------------|---------------------------------------|-------------------|
| Morphine <sup>a</sup> | Parenteral              | 60 mg (IM, SC, IV)                    | 10 mg q 3-4 h SC  |
| Morphine <sup>a</sup> | Oral                    | 180 mg                                | 30 mg q 4-6 h PO  |
| Codeine               | Oral                    | 1200 mg                               | 200 mg q 4-6 h PO |
| Codeine               | Parenteral              | --                                    | 120 mg SC         |
| Fentanyl              | Patch                   | 50 to 100 mcg/h patch (change q 72 h) |                   |
| Fentanyl              | Parenteral              | --                                    | 0.1 mg IM q 1-2 h |
| Hydrocodone           | --                      | NC                                    | NC                |
| Hydromorphone         | Parenteral              | 9-12 mg IM, SC, IV                    | 1.5 mg q 3-4 h SC |
| Hydromorphone         | Oral                    | 45-60 mg                              | 3 mg q 4-6 h PO   |
| Levorphanol           | Parenteral              | --                                    | 2 mg q 4-5 h SC   |
| Levorphanol           | Oral                    | --                                    | 4 mg q 4-6 h PO   |
| Meperidine            | Oral                    | --                                    | 300 mg q 3-4 h PO |
| Meperidine            | Parenteral              | --                                    | 75 mg q 2-3 h SC  |
| Methadone             | Oral                    | 10-40 mg                              | 20 mg q 4-6 h PO  |
| Methadone             | Parenteral              | --                                    | 10 mg IM q 4-5 h  |
| Oxycodone             | Oral                    | 120 mg                                | 30 mg q 4-5 h PO  |

<sup>a</sup>Morphine is the standard used for comparison to other drugs. IM = intramuscular, IV = intravenous, NC = no consensus, PO = by mouth, SC = subcutaneous

## COMPOUNDED FORMULAS FOR PAIN

Note: Other drugs (and appropriate doses) can be used in these dosage forms.

### Rx

Morphine Sulfate 10-g and Dextromethorphan Hydrobromide 30-mg Capsules

### Rx

Morphine Sulfate 2.5-mg/mL Sterile Inhalation Solution

### Rx

Fentanyl Citrate 25-mcg/0.1-mL Nasal Spray

### Rx

Morphine Sulfate 50-mg Slow-Release Suppository

### Rx

Morphine Sulfate 50-mg/mL and Bupivacaine Hydrochloride 25-mg/mL Sterile Solution for Ambulatory Pump

### Rx

Morphine Sulfate 20-mg and Prochlorperazine Maleate 10-mg Troches

### Rx

Fentanyl 0.2-mg Lollipops

### Rx

Fentanyl Citrate 50-mcg Chewable Gummy Gels

### Rx

Methadone Hydrochloride 25-mg Chewing Gum

### Rx

Morphine Sulfate 50-mg/mL in Pluronic Lecithin Organogel Transdermal Gel

### Rx

Fentanyl 100-mcg/0.1-mL and Promethazine Hydrochloride 12.5-mg/0.1-mL in Pluronic Lecithin Organogel Transdermal Gel

### Rx

Methadone Hydrochloride 1-mg/mL and Gabapentin 50-mg/mL in Pluronic Lecithin Organogel Transdermal Gel

**TABLE 2. ANALGESIC EQUIVALENT DOSES.<sup>2,3</sup>**

| DRUG NAME              | DOSE                                             |
|------------------------|--------------------------------------------------|
| Buprenorphine          | 0.4 mg IM                                        |
| Butorphanol            | 2 mg IM                                          |
| Codeine                | 120 mg IM                                        |
| (Tylenol with Codeine) | 200 mg PO                                        |
| Fentanyl               | 0.1 mg IM                                        |
| Hydromorphone          | 1.5 mg IM<br>3-7.5 mg PO                         |
| Levorphanol            | 2 mg IM A 1 mg IM C<br>4 mg PO A 1 mg PO C       |
| Methadone              | 10 mg IM A 2-4 mg IM C<br>20 mg PO A 2-4 mg IM C |
| Meperidine             | 75 mg IM<br>300 mg PO                            |
| Morphine               | 10 mg IM<br>30 mg PO C 60 mg PO A                |
| Nalbuphine             | 10 mg IM                                         |
| Oxycodone              | 20-30 mg PO                                      |
| (5 mg in Percocet)     |                                                  |
| Oxymorphone            | 1 mg IM<br>10 mg PO                              |
| Sufentanil             | 0.02 mg IM                                       |

A = acute dosing, C = chronic dosing, IM = intramuscular, PO = by mouth, SC = subcutaneous