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Equianalgesic Dosing of Opioids for Pain Management

Equianalgesic doses contained in this chart are approximate, and should be used only as a guideline. Dosing must be titrated to individual response. There is often incomplete cross-tolerance among these drugs. ***It is, therefore, recommended to begin with a 50% lower dose than the equianalgesic dose when changing drugs and then titrate*** *to a safe/effective response.*[1,3,4,34] *Dosing adjustments for renal or hepatic insufficiency, cytochrome P450 drug interactions, genetics, and other conditions or medications that affect drug metabolism, kinetics, or response may also be necessary.*[2,34,48,53] *Also consider pain control at time of switch.*[4,5] *In general, use cautious dosing for elderly or debilitated patients, and patients with renal or hepatic impairment.*[48] *Some products have specific dosing recommendations for these populations (****see footnotes****). See our* Opioid Conversion Algorithm *for instructions on converting from one opioid to another*.

A website with an equianalgesic dose calculator is available at http://www.hopweb.org

Drug[f,i,k,L]	**Equianalgesic Doses (mg)**[1,3,4]		**Approximate Equianalgesic 24 hr Dose (Assumes Around-the-Clock Dosing)**[g]		**Usual Starting Dose (Opioid-Naïve Adults) (Doses NOT Equianalgesic)**	
	Parenteral	**Oral**	**Parenteral**	**Oral**	**Parenteral**	**Oral**
Morphine (immediate-release tablets, oral solution, injection)[k,L]	10	30	3-4 mg q 4 h	10 mg q 4 h	2.5 mg q 4 h[50]	10 mg q 4 h (acute or chronic pain)[40,41,51, j] 2-10 mg q 4 h (hospice)[5]
Controlled-release morphine (e.g., *MS Contin, Kadian*)	NA	30	NA	30 mg q 12 h (*Kadian* may be given as 60 mg q 24 h)[6,21]	NA	*MS Contin* (U.S.): 15 mg q 12 h[29, j] *MS Contin* (Canada): 30 mg q 12 h[57, j] Other products not for initial dosing.[6,21,29,h, j]
Extended-release morphine (*Avinza* [U.S.], *Embeda* [with naltrexone, U.S.])	NA	30	NA	60 mg q 24 h (*Embeda* may be given as 30 mg q 12 h)[12]	NA	*Avinza*: 30 mg q 24 h[7, j] *Embeda*: 20 mg q 24 h[12, j]

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Drug[f,i,k,L]	**Equianalgesic Doses (mg)**[1,3,4]		**Approximate Equianalgesic 24 hr Dose (Assumes Around-the-Clock Dosing)**[g]		**Usual Starting Dose (Opioid-Naïve Adults) (Doses NOT Equianalgesic)**	
	Parenteral	**Oral**	**Parenteral**	**Oral**	**Parenteral**	**Oral**
Hydromorphone (*Dilaudid*)	1.5-2	7.5-8	0.5-0.8 mg q 4 h	2-4 mg q 4 h	See footnotes a,d.	See footnote a.
Controlled-release hydromorphone (*Hydromorph Contin* [Canada])	NA	7.5	NA	6 mg q 12 h	NA	3 mg q 12 h[30, j]
Extended-release hydromorphone (*Exalgo*, *Jurnista* [Canada])	NA	See footnote b.	NA	See footnote b.	NA	See footnotes e, h, and j.
Oxycodone (e.g., *Roxicodone* [U.S.], *Oxecta* [U.S.], *Oxy IR* [Canada], also in *Percocet*, others)	NA	20-30	NA	5-10 mg q 4 h	NA	5-15 mg q 4-6 h (acute or chronic pain)[42,43] (**Product labeling**) 5-10 mg q 8-12 h[14] or 5 mg q 4-6 h[41] (chronic noncancer pain) (**Guidelines**)
Controlled-release oxycodone (*OxyContin* [U.S.], *OxyNeo* [Canada])	NA	20-30	NA	20-30 mg q 12 h	NA	10 mg q 12 h[9, j]
Extended-release oxycodone and acetaminophen (*Xartemis XR* [U.S.])	Indicated for acute pain only. Not interchangeable with other products due to differing pharmacokinetics. Dose is two tablets every 12 hours. Each tablet contains oxycodone 7.5 mg and acetaminophen 325 mg. The second dose may be taken as early as eight hours after the first dose if needed, but subsequent doses should be taken every 12 hours.[59]					

Drug[f,i,k,L]	**Equianalgesic Doses (mg)**[1,3,4]		**Approximate Equianalgesic 24 hr Dose (Assumes Around-the-Clock Dosing)**[g]		**Usual Starting Dose (Opioid-Naïve Adults) (Doses NOT Equianalgesic)**	
	Parenteral	**Oral**	**Parenteral**	**Oral**	**Parenteral**	**Oral**
Oxymorphone (*Opana* [U.S.])	1	10	0.3-0.4 mg q 4 h	5 mg q 6 h	0.5 mg q 4-6 h[10]	10-20 mg q 4-6 h (acute pain)[44,r] 5-10 mg q 4-12 h (chronic noncancer pain)[14,41]
Extended-release oxymorphone (*Opana ER* [U.S.])[c,q]	NA	10	NA	10 mg q 12 h	NA	5 mg q 12 h[11, j]
Extended-release hydrocodone (*Zohydro ER* [U.S.])	NA	See footnotes.	NA	See footnotes.	NA	10 mg q 12 h[58, j]
Hydrocodone (in *Norco* [U.S.], others)	NA	30-45	NA	10-15 mg q 4 h	NA	5-10 mg q 4-6 h (moderate to moderately severe pain)[45] 5-10 mg q 4-12 h (chronic noncancer pain)[14,41]
Codeine[n]	100-130	200	30-50 mg q 4 h	60 mg q 4 h	10 mg q 3-4 h[52]	15-60 mg q 4 h (mild to moderately severe pain)[46] 15-30 mg q 4-12 h (chronic noncancer pain)[14,41]
Controlled-release codeine (*Codeine Contin* [Canada])[m,n]	NA	200	NA	180 mg q 12 h	NA	50 mg q 12 h[49]

Drug[f,i,k,L]	**Equianalgesic Doses (mg)**[1,3,4]		**Approximate Equianalgesic 24 hr Dose (Assumes Around-the-Clock Dosing)**[g]		**Usual Starting Dose (Opioid-Naïve Adults) (Doses NOT Equianalgesic)**	
	Parenteral	**Oral**	**Parenteral**	**Oral**	**Parenteral**	**Oral**
Methadone (*Dolophine* [U.S.], *Metadol* [Canada])[o]	Variable	Variable	For opioid-tolerant patients only.[14] The conversion ratio of methadone is highly variable depending on factors such as patient tolerance, morphine dose, and length of dosing (short-term versus chronic dosing). Because the analgesic duration of action is shorter than the half-life, toxicity due to drug accumulation can occur with just a few doses.[35] For conversion methods, see http://www.cancer.gov/cancertopics/pdq/supportivecare/pain/HealthProfessional/page3. Some experts recommend that only those with substantial experience with its use should prescribe methadone.[39,55]			
Meperidine (*Demerol*)	75	300	Should be used for acute dosing only (short duration of action [2.5 to 3.5 hours]) and neurotoxic metabolite, normeperidine.[1] Avoid in renal insufficiency and use caution in hepatic impairment and in the elderly (potential for toxicity due to accumulation of normeperidine).[1,16-18] Seizures, myoclonus, tremor, confusion, and delirium may occur.[1]			
Fentanyl[p]	0.1	NA	All noninjectable fentanyl products are for opioid-tolerant patients only. Do not convert mcg for mcg among fentanyl products (i.e., patch, transmucosal lozenge [*Actiq* (U.S.)], buccal tablet [*Fentora* (U.S.)], buccal film [*Onsolis*], nasal spray [*Lazanda* (U.S.)], sublingual tablet [*Abstral*]). See specific product labeling (U.S.: Drugs@FDA; Canada: Health Canada Drug Product Database) for dosing. Or, for U.S. products only, see our *PL Chart*, *Fentanyl Products for Breakthrough Pain*. Because product labeling recommendations might underdose patients with chronic pain, some experts use this conversion in cancer patients: oral morphine 60 mg total daily dose = 25 mcg/hr fentanyl patch. Round up or down based on patient factors and available patch sizes.[56] Use clinical judgment.			

NA = not available.

Most of the above oral opioids are available as generics. Exceptions (prices are wholesale average cost [U.S.]) include: *Opana ER* ($3.63/10 mg tab), *OxyContin* ($2.28/10 mg tab), *Embeda* ($4.15/20 mg cap), *Exalgo* ($11.32/8 mg tab), *Zohydro ER* ($6.67/10 mg cap [retail]). *Xartemis XR* ($2.30/tab). As a comparison, generic morphine controlled-release = $1.14/30 mg tab.

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a. Product labeling for **hydromorphone** recommends a starting dose of 0.2 mg to 1 mg IV every two to three hours (Canadian monograph: 2 mg IV every four to six hours) as needed, or 2 mg to 4 mg orally every four to six hours as needed.[8,15,20] An even lower oral starting dose (2 mg two or three times daily) has been recommended for chronic pain in opioid-naïve patients.[14] Some institutions use even lower doses of parenteral hydromorphone (e.g., 0.2 mg to 0.5 mg every two hours as needed). One regimen starts opioid-naïve patients at 0.2 mg IV every two hours as needed for mild or moderate pain, with the option in moderate pain to give an extra 0.2 mg after 15 minutes if relief is inadequate after the first 0.2 mg dose. For severe pain, 0.5 mg IV every two hours as needed is used initially. In adults <65 years of age, the 0.5 mg dose can be repeated in 15 minutes if relief is inadequate, for a maximum of 1 mg in two hours.

b. Per the product labeling, convert to ***Exalgo*** 12 mg *from* oral codeine 200 mg, hydrocodone 30 mg, morphine 60 mg, oxycodone 30 mg, oxymorphone 20 mg, or transdermal fentanyl 25 mcg/hr. (These conversion doses should NOT be used when switching from *Exalgo* to another opioid.) After 50% dose reduction for incomplete cross-tolerance, reduce dose again by 50% for moderate renal impairment, and by 75% for severe renal or moderate hepatic impairment. Not for use in severe hepatic impairment.[13] The ***Jurnista*** product monograph recommends a 5:1 oral morphine:oral hydromorphone conversion ratio.[19] When converting from immediate-release hydromorphone, the *Jurnista* dose should be rounded down.[19]

c. Per the product labeling, oral **oxymorphone** 10 mg ER is approximately equivalent to hydrocodone 20 mg or oxycodone 20 mg.[11]

d. ***Dilaudid*** Canadian monograph recommends parenteral starting dose of 2 mg.[20] See footnote "a" for additional information and precautions.

e. No initial dose for ***Exalgo***. For opioid-tolerant patients only.[13] Initial ***Jurnista*** dose (opioid-naïve or <40 mg daily oral morphine equivalents) is 4 to 8 mg q 24 h.[19]

f. **Tramadol** (e.g., *Ultram*, *Ralivia* [Canada]), potency is about one-tenth that of morphine, similar to codeine.[1] The maximum daily dose of tramadol is 300 mg to 400 mg, depending on the product.[22-28,36,37] See product labeling for dosing in elderly, or in renal or hepatic dysfunction.

g. Examples of doses seen in clinical practice, taking into account available dosage strengths.

h. Labeling for some products (*Kadian*, *Jurnista* [Canada]) recommends beginning treatment with an immediate-release formulation.[6,19,21,29]

i. **Tapentadol** controlled-release (*Nucynta CR*, Canada) and oxycodone controlled-release exhibit comparable pain relief in a dose ratio of 5:1 (tapentadol:oxycodone).[31] The maximum dose of tapentadol CR is 250 mg twice daily.[31] No specific dose conversion is given for *Nucynta* (U.S.), *Nucynta IR* (Canada), and *Nucynta ER* (U.S.).[32,33] Not for use in severe renal or hepatic dysfunction.[31-33,38]

j. Some experts do not recommend for chronic pain in opioid-naïve patients.[14]

k. The initial dose of transdermal **buprenorphine** (*Butrans*) for patients taking less than 30 mg of oral morphine or equivalent per day is a 5 mcg/hr patch applied once weekly (Canada: start with 5 mcg/hr patch in opioid-naïve patients, and 5-10 mcg/hr patch in patients taking up to 80 mg oral morphine equivalents per day).[47,60] U.S.: When converting from 30 to 80 mg of oral morphine equivalents daily dose, first taper to 30 mg oral morphine equivalents per day, then start with the 10 mcg/hr patch.[60] The maximum dose is one 20 mcg/hr patch once weekly.[47,60]

L. Parenteral morphine 10 mg is approximately equal to parenteral **pentazocine** 60 mg, oral pentazocine 180 mg, parenteral **butorphanol** 2 mg, and parenteral **nalbuphine** 10 mg.[49] For buprenorphine transdermal patch (*Butrans*), see footnote "k." The analgesic efficacy of these drugs is limited by a dose ceiling. Furthermore, the mixed agonists-antagonists (i.e., pentazocine, butorphanol, nalbuphine) are contraindicated for use in patients receiving an opioid agonist because they can precipitate withdrawal and increase pain. They also pose a risk of psychotomimetic effects.[1]

m. Reduce dose by 25% when switching from oral **codeine** phosphate to account for phosphate content of tablet.[49]

n. Analgesic efficacy limited by a dose ceiling.[46,49]

o. Relatively safe choice in renal or liver insufficiency.[54,55]
p. Relatively safe choice in renal or liver insufficiency.[55] Clearance reduced by uremia.[54] Do not start with patch in renal or liver failure.[54] Watch for delayed toxicity.[54,55]
q. *Opana ER* has received a notice of compliance (June 2012) by Health Canada. At time of publication, it is not yet available on the Canadian market.
r. Start with an oral dose of 5 mg q 4-6 h for opioid-naïve elderly or opioid-naïve patients with renal or liver impairment.[44]
s. Conversion factors for converting to ***Zohydro ER*** are 1 for hydrocodone or oxycodone; 2 for oxymorphone; 2.67 for hydromorphone; 0.67 for morphine; and 0.1 for codeine. Sum the current total daily dose of opioid, then multiply by the conversion factor to get the total daily *Zohydro ER* dose. Round down. Divide q 12 h.[58] (Conversion factors should NOT be used to switch from *Zohydro ER* to another opioid.)

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References

1. National Cancer Institute Pain (PDQ). Pharmacologic management. http://www.cancer.gov/cancertopics/pdq/supportivecare/pain/HealthProfessional/page3. (Accessed March 12, 2014).
2. Pergolizzi J, Boger RH, Budd K, et al. Opioids and the management of chronic severe pain in the elderly: consensus statement of an international expert panel with focus on the six clinically most often used World Health Organization step III opioids (buprenorphine, fentanyl, hydromorphone, methadone, morphine, oxycodone). *Pain Pract* 2008;8:287-313.
3. Agency for Healthcare Research and Quality. Morbidity & mortality rounds on the web. Case & commentary. Strassels SA. Miscalculated risk. Hospital medicine. August 2006. http://webmm.ahrq.gov/case.aspx?caseID=132#table1. (Accessed March 12, 2014).
4. American Academy of Hospice and Palliative Medicine. Key principles of opioid administration. http://www.aahpm.org/pdf/equianalgesictable.pdf. (Accessed March 12, 2014).
5. American Academy of Hospice and Palliative Medicine. Guidelines for prescribing opiates for hospice and palliative care patients. http://www.aahpm.org/pdf/guidelinesforopioids.pdf. (Accessed March 12, 2014).
6. Product information for *Kadian*. Actavis Kadian LLC. Morristown, NJ 07960. April 2014.
7. Product information for *Avinza*. King Pharmaceuticals, Inc. Bristol, TN 37620. April 2014.
8. Product information for *Dilaudid* injection. Purdue Pharma L.P. Stamford, CT 06901. June 2011.
9. Argoff CE, Silvershein DI. A comparison of long- and short-acting opioids for the treatment of chronic noncancer pain: tailoring therapy to meet patient needs. *Mayo Clin Proc* 2009;84:602-12.
10. Product information for *Opana* injection. Endo Pharm. Chadds Ford, PA 19317. February 2013.
11. Product information for *Opana ER*. Endo Pharm. Chadds Ford, PA 19317. April 2014.
12. Product information for *Embeda*. Pfizer Inc. New York, NY 10017. April 2014.
13. Product information for *Exalgo*. Mallinckrodt Brand Pharmaceuticals, Inc.. Hazelwood, MO 63042. April 2014.
14. Manchikanti L, Abdi A, Atluri S, et al. American Society of Interventional Pain Physicians (ASIPP) guidelines for responsible opioid prescribing in chronic non-cancer pain: part 2-guidance. *Pain Physician* 2012;15(3 Suppl):S67-S116.
15. Product information for *Dilaudid* oral liquid and tablets. Purdue Pharma L.P. Stamford, CT 06901. June 2013.
16. Product information for *Demerol*. Sanofi-aventis U.S. Bridgewater, NJ 08807. November 2011.
17. Fulton CW. Limiting meperidine use in pain management. *Hosp Pharm* 2001;36:1214,1217-8.
18. *PL Detail-Document*, Pharmacotherapy Choices for Patients with Dementia. *Pharmacist's Letter/Prescriber's Letter*. May 2008.
19. Product monograph for *Jurnista*. Janssen-Ortho Inc. Toronto, ON M3C 1L9. November 2013.
20. eCPS [Internet]. Ottawa (ON): Canadian Pharmacists Association c2014. *Dilaudid* monograph (April 2012). http://www.e-therapeutics.ca. (Accessed March 12, 2014).
21. Product monograph for *Kadian*. Abbott Labs. Vaughan, ON L4K 4T7. December 2006.
22. Product information for *Ultram*. Janssen Pharmaceuticals Inc. Titusville, NJ 08560. February 2013.
23. Product information for *Ultracet*. Janssen Pharmaceuticals Inc. Titusville, NJ 08560. November 2013.
24. Product information for *Ultram ER*. Janssen Pharmaceuticals Inc. Titusville, NJ 08560. February 2013.
25. Product monograph for *Ralivia*. Valeant Canada LP. Montreal, QC H4R 2P9. February 2011.
26. Product monograph for *Tramacet*. Janssen-Ortho Inc. Toronto, ON M3C 1L9. July 2013.
27. Product monograph for *Zytram XL*. Purdue Pharma. Pickering, ON L1W 3W8. January 2014.
28. Product monograph for *Tridural*. Labopharm Inc. Laval, QC H7V 4B4. January 2013.
29. Product information for *MS Contin*. Purdue Pharma, L.P. Stamford, CT 06901. April 2014.
30. Product monograph for *Hydromorph Contin*. Purdue Pharma. Pickering, ON L1W 3W8. October 2012.
31. Product monograph for *Nucynta CR*. Janssen. Toronto, ON M3C 1L9. March 2014.
32. Product information for *Nucynta ER*. Janssen. Titusville, NJ 08560. April 2014.
33. Product information for *Nucynta*. Janssen Pharmaceuticals, Inc. Titusville, NJ 08560. October 2013.
34. FDA. Introduction for the FDA blueprint for prescriber education for extended-release and long-acting opioid analgesics. April 2013. http://www.fda.gov/downloads/Drugs/DrugSafety/InformationbyDrugClass/UCM277916.pdf. (Accessed March 12, 2014).
35. *PL Detail-Document*, Methadone: Focus on Safety. *Pharmacist's Letter/Prescriber's Letter*. September 2006.
36. Product monograph for *Durela*. Cipher Pharmaceuticals Inc. Mississauga, ON L4W 4P1. January 2014.
37. Product monograph for *Ultram*. Janssen Inc. Toronto, ON M3C 1L9. July 2013.
38. Product monograph for *Nucynta IR*. Janssen Inc. Markham, ON L3R 0T5. March 2014.
39. Centers for Disease Control and Prevention (CDC). Vital signs: risk of overdose from methadone used

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for pain relief-United States, 1999-2010. *MMWR Morb Mortal Wkly Rep* 2012;61:493-7.
40. Product information for morphine solution. Roxane Laboratories, Inc. Columbus, OH 43216. January 2012.
41. Sundwall DN, Rolfs RT, Johnson E. Utah Department of Health. Utah clinical guidelines on prescribing opioids for treatment of pain. 2009. http://www.dopl.utah.gov/licensing/forms/OpioidGuidlines.pdf. (Accessed March 12, 2014).
42. Product information for *Oxecta*. King Pharmaceuticals Inc. Bristol, TN 37620. January 2014.
43. Product monograph for *Oxy IR*. Purdue Pharma. Pickering, ON L1W 3W8. June 2012.
44. Product information for *Opana* tablets Endo Pharmaceuticals Inc. Chadds Ford, PA 19317. March 2013.
45. Product information for *Norco*. Watson Pharma Inc. Corona, CA 92880. June 2011.
46. Product information for codeine sulfate tablets. Roxane Laboratories, Inc. Columbus, OH 43228. April 2013.
47. Product monograph for *BuTrans*. Purdue Pharma. Pickering, ON L1W 3W8. March 2012.
48. *PL Detail-Document*, Opioids for Chronic Non-cancer Pain. *Pharmacist's Letter/Prescriber's Letter*. September 2010.
49. Product monograph for *Codeine Contin*. Purdue Pharma. Pickering, ON L1W 3W8. September 2013.
50. eCPS [Internet]. Ottawa (ON): Canadian Pharmacists Association c2014. *Opioids* monograph (July 2013). http://www.e-therapeutics.ca. (Accessed March 12, 2014).
51. eCPS [Internet]. Ottawa (ON): Canadian Pharmacists Association c2014. *MS IR* monograph (September 2012). http://www.e-therapeutics.ca. (Accessed March 12, 2014).
52. Ballantyne JC, Mao J. Opioid therapy for chronic pain. *N Engl J Med* 2003;349:1943-53.
53. *PL Detail-Document*, Codeine Safety in Kids. *Pharmacist's Letter/Prescriber's Letter*. April 2013.
54. Induru RR, Lagman RL. Managing cancer pain: frequently asked questions. *Cleve Clin J Med* 2011;78:449-64.
55. Carbonara GM. Opioids in patients with renal or hepatic dysfunction. *Practical Pain Management.* May 1, 2008. http://www.practicalpainmanagement.com/treatments/pharmacological/opioids/opioids-patients-renal-hepatic-dysfunction?page=0,0. (Accessed March 12, 2014).
56. Skaer TL. Transdermal opioids for cancer pain. *Health Qual Life Outcomes* 2006;4:24.
57. Product monograph for *MS Contin*. Purdue Pharma. Pickering, ON L1W 3W8. October 2012.
58. Product information for *Zohydro ER*. Zogenix. San Diego, CA 92130. October 2013.
59. Product information for *Xartemis XR*. Mallinckrodt Brand Pharmaceuticals, Inc. Hazelwood, MO 63042. March 2014.
60. Product information for *Butrans*. Purdue Pharma. Stamford, CT 06901-3431. April 2014.

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