Eastern Metropolitan Region
Palliative Care Consortium

Opioid Conversion Ratios
Guide to Palliative Care Practice 2016

3/5/2016

Consortium Manager

Eastern Metropolitan Region Palliative Care Consortium
PO Box 2110
Rangeview 3132
Victoria
Australia

It is highly recommended this guide is printed in colour, to aid ease of use.

The access point for the current electronic version of the guide is
Eastern Metropolitan Region Palliative Care Consortium www.emrpcc.org.au or Centre for Palliative Care www.centreforpallcare.org
Printed versions can only be considered up-to-date for a period of one month from the printing date after which, the latest version should be downloaded

ACKNOWLEDGEMENTS

EMRPCC Opioid Conversion Guide Review 2016
Project officer: Ms S Scholes, *BPharm Grad Cert Heath (Palliative Care) MSHP*

Victorian Palliative Medicine Specialists: Dr P Poon; Dr M Benson; Dr M Franco and Dr L William who provided fresh perspectives on the 2016 document.

EMRPCC Clinical Group (2016):

Eastern Health: Dr L William (Palliative Medicine Specialist), Ms J Wilkinson & Ms D Bach (Clinical Nurse Consultants)
Eastern Palliative Care Association Inc: Mr D Halliwell (Clinical Nurse Consultant)
St Vincent's Health Melbourne & Eastern Palliative Care Association Inc: Dr P Sherwen (Palliative Medicine Specialist)
St Vincent's Health Melbourne: Mr T Whelan (Nurse Practitioner)
Eastern Metropolitan Region Palliative Care Consortium: Ms C Clifton (Consortium Manager)

Special Acknowledgments:
Ms A Padrissa & Ms K McGrath, Eastern Health (Wantirna Health) Palliative Care Pharmacists
Ms S Chung, St Vincent's Hospital (Melbourne), Medicines Information Pharmacist (Covering)

Acknowledgement for previous documents:
Acknowledgment is also extended to the original 2008 EMRPCC clinical group and all contributors to the initial EMRPCC Opioid Conversion Ratios – Guide to Practice (October 2008) and the members of the EMRPCC clinical groups who revised the document EMRPCC Opioid Conversion Ratios- Guide to Practice (December 2010 and again in July 2013).

The EMRPCC welcomes feedback. Please send comments to:
Consortia Manager, Eastern Metropolitan Region Palliative Care Consortium
PO Box 2110 Rangeview Victoria Australia 3132 or email consortiummanager@epc.asn.au

Contents

DISCLAIMER

The information in this document is to be used as a guide to practice only. It is the responsibility of the user to ensure the information is used correctly. This guide reflects current palliative care practice in the Eastern Metropolitan Region of Melbourne and published evidence at the time of the review. The current electronic version of the document is available at www.emrpcc.org.au and should always be referred to.

All medication doses derived from this guide to practice, should be checked and prescribed by a medical doctor or nurse practitioner with appropriate experience in opioid prescribing. Opioids may be given via different routes as part of clinical practice, to reflect clinical needs, however not all routes (e.g. intrathecal) have been covered in this guide.

Medication doses should be modified in response to the patient/client's clinical situation and status, including previous exposure to opioids and concurrent medications. All patients should be monitored closely until stable when commencing, adjusting dosage and/or switching opioid medications. Adhere to all legislation and professional requirements including organisational policies and procedures regarding opioid medications and their administration.

GENERAL NOTES

- The conversions are applicable in pain for palliative care patients rather than patients with chronic pain
- **It is recommended that opioids be converted to the equianalgesic oral morphine as the first step, except when converting from the same drug to the same drug (e.g. oral to subcutaneous)**
- When converting, calculate the equianalgesic starting dose of the new opioid using the guidelines
- Apply a dose reduction of 25% to 50% to the equianalgesic starting dose to allow for cross-tolerance
- A dose reduction closer to 50% is appropriate if the patient is elderly or medically frail
- Also consider
    - dose and duration of previous opioid treatment
    - current pain severity
    - patient's ethnicity, for example, oxycodone may be metabolised differently by Caucasian, Asian and North African groups due to genetic polymorphism
    - renal function, for example, use caution in mild to moderate renal impairment with hydromorphone, morphine and oxycodone. Consensus guidelines suggest fentanyl is the opioid of choice in severe renal impairment
    - hepatic function, for example, decrease the dose and frequency of administration of morphine in hepatic failure, and avoid oxycodone in severe cirrhosis. Fentanyl is preferred in moderate to severe liver failure or cirrhosis
    - occurrence of adverse effects
    - direction of switch of opioid, e.g. methadone to morphine
- Prescribe prn breakthrough opioid during the titration process of 1/10th to 1/6th of the total daily opioid dose
- Frequently monitor for patient response and individual dose titration

(References 1,2,3)

ORAL MORPHINE TO OTHER ORAL OPIOIDS				
Oral To Oral	**Conversion Ratio**	**Example**	**Comments**	**Reference**
Morphine to Codeine	1:10	Oral Morphine 6mg = Oral Codeine 60mg	**Avoid conversion and treat as opioid naïve** Codeine has a limited role in managing moderate-severe pain in palliative care	3,4,5,6
Morphine to Hydromorphone	5:1	Oral Morphine 5mg = Oral Hydromorphone1mg		3,4,5
Morphine to Methadone	**Palliative Care Specialist input required** See Methadone on pages 8-9 for more information			
Morphine to Oxycodone	1.5:1	Oral Morphine 15mg = Oral Oxycodone 10 mg	The oxycodone component of Targin® should be considered in conversions. If doses greater than Targin® 80/40 mg per day are required, single entity modified release oxycodone should be used. Note the beneficial effect of naloxone on bowel function may be impaired	3,4,5,6,7
Morphine to Tapentadol	1:3	Oral Morphine 100mg = Oral Tapentadol 300mg		3,8,9
Morphine to Tramadol	1:5 to 1:10	Oral Morphine 10mg = Oral Tramadol 50 to100mg	Tramadol has a limited role in managing moderate to severe pain in palliative care	3,4,6

ORAL OPIOIDS TO SUBCUTANEOUS OPIOIDS– same drug to same drug					
Oral	**Subcutaneous**	**Conversion Ratio**	**Example**	**Comments**	**Reference**
Morphine	Morphine	2:1 to 3:1	Oral Morphine 30mg = Subcutaneous Morphine 10 to 15mg		3,4,6
Oxycodone	Oxycodone	1.5:1 to 2:1	Oral Oxycodone 30mg = Subcutaneous Oxycodone 15 to 20mg		3,4,6
Hydromorphone	Hydromorphone	2:1 to 3:1	Oral Hydromorphone 15mg = Subcutaneous Hydromorphone 5 to 7.5mg		3,4,6

SUBCUTANEOUS MORPHINE TO OTHER SUBCUTANEOUS OPIOIDS					
Subcutaneous	**Subcutaneous**	**Conversion Ratio**	**Example**	**Comments**	**Reference**
Morphine	Fentanyl	100:1	Subcutaneous Morphine 10,000 micrograms (10mg) = Subcutaneous Fentanyl 100 micrograms	The 100:1 conversion ratio is conservative	3,10
Morphine	Hydromorphone	5:1	Subcutaneous Morphine 10mg = Subcutaneous Hydromorphone 2mg		3,4,6
Morphine	Oxycodone	1:1	Subcutaneous Morphine 10mg = Subcutaneous Oxycodone 10mg		3,4
Morphine	Sufentanil	1000:1	Subcutaneous Morphine 10,000micrograms (10mg) = Subcutaneous Fentanyl 100micrograms = Subcutaneous Sufentanil 10micrograms	Convert to fentanyl initially	11

MORPHINE TO TRANSDERMAL FENTANYL				
Oral Morphine (mg/24 hours)	**Subcutaneous Morphine (mg/24 hrs) (Dose ratio 3:1 to 2:1)**	**Transdermal Fentanyl (mcg/24 hours) (Dose ratio from oral morphine 100:1)**	**Transdermal Fentanyl (mcg/ hour) Patch Size**	**Reference**
30	10 to 15	300	12	3,12
60	20 to 30	600	25	3,12
120	40 to 60	1200	50	3,12
180	60 to 90	1800	75	3,12
240	80 to 120	2400	100	3,12
Seek specialist palliative care advice when converting at high doses				

CONVERSION GUIDE FOR OPIOID TO TRANSDERMAL FENTANYL	
From	**To Transdermal Fentanyl**
4 hour immediate release (IR) oral opioid	Give regular doses IR oral opioid for the first 12 hours after applying patch
12 hour controlled release (CR) long acting oral opioid	Apply the patch at the same time as administering the final 12 hour (CR) dose
24 hour controlled release (CR) long acting oral opioid	Apply the patch twelve hours after administering the final 24 hour (CR) dose
Continuous subcutaneous infusion morphine (syringe driver)	Continue the syringe driver unchanged for 8 to 12 hours after applying the patch, then cease
Continuous subcutaneous infusion fentanyl (syringe driver)	Continue the syringe driver at the same rate for 6 hours after applying the patch, then cease
Effective systemic analgesic concentrations are generally reached in less than 12 hours for fentanyl after applying patch (4,13)	

SUBCUTANEOUS FENTANYL TO TRANSDERMAL FENTANYL - same drug to same drug				
Subcutaneous	**Transdermal**	**Conversion Ratio**	**Example**	**Reference**
Fentanyl	Fentanyl	1:1	Fentanyl 600micrograms / 24 hours = Fentanyl patch 25micrograms/hour	10,14

TRANSMUCOSAL FENTANYL
Fentanyl transmucosal products (e.g. lozenges, sublingual and orally-disintegrating tablets) are available for breakthrough cancer pain not adequately managed by other short acting opioids. These products are not interchangeable as they have different pharmacokinetics, therefore titration from baseline (de novo) is required when switching products.
Transmucosal fentanyl products offer a faster onset of relief than oral morphine in breakthrough pain and should only be used in patients who are already receiving opioids and are opioid tolerant. A patient should be receiving at least 60mg of oral morphine equivalents per day or 25 to 50 micrograms transdermal fentanyl per hour, if transmucosal fentanyl is to be considered for breakthrough pain. There is no direct conversion ratio between morphine and transmucosal fentanyl. Refer to Product Information and the Pharmaceutical Benefits Scheme for further information

TRANSDERMAL BUPRENORPHINE TO ORAL MORPHINE					
Patch Strength	**Delivery Rate**	**Conversion Ratio**	**Calculation**	**Comments**	**Reference**
Buprenorphine 5mg / 7 days (120 micrograms / 24 hours)	5 micrograms / hour	1:75 – 1:100	5mg patch = 5 micrograms buprenorphine per hour 5mcg x 24 = 120 micrograms over 24 hours 120microgram buprenorphine x 75 = 9,000 micrograms (9 mg) or x 100 = 12,000 micrograms (12mg) of oral morphine	Oral Morphine dose 9 to 12mg/24hours	3,5
Buprenorphine 10mg / 7 days (240 micrograms / 24 hours)	10 micrograms / hour	1:75 – 1:100	10mg patch = 10micrograms buprenorphine per hour 10microgram x 24 = 240micrograms over 24 hours 240microgram buprenorphine x 75 = 18,000micrograms (18mg) or x 100 = 24,000micrograms (24 mg) of oral morphine	Oral Morphine dose 18 to 24mg/24 hours	3,5
Buprenorphine 20mg / 7 days (480 micrograms / 24 hours)	20 micrograms / hour	1:75 – 1:100	20mg patch = 20micrograms buprenorphine per hour 20microgram x 24 = 480micrograms over 24 hours 480 mcg buprenorphine x 75 = 36,000 micrograms (36mg) or x 100 = 48,000micrograms (48 mg) of oral morphine	Oral Morphine dose 36 to 48mg/24 hours Maximum transdermal dose recommended is 40 micrograms/hour (2 x 20mg/7day patches)	3,4,5
Breakthrough pain is treated with an immediate release opioid e.g. morphine or oxycodone. Respiratory depression is rare in the doses of buprenorphine used in palliative care practice in Australia. On removal of the buprenorphine patch, a short acting opioid should be prescribed for the initial 24 hours and a long acting opioid commenced after 24hours					3,4

METHADONE

Conversion to methadone from other opioids is complex, and <u>should not be attempted without consultation</u> with a specialist experienced in the use of methadone. Palliative care consultation is of particular importance for the higher doses of opioid and the frail or elderly patient. It is strongly recommended that methadone therapy be initiated in the inpatient setting where patients can be closely monitored for signs of cumulative toxicity (commonly sedation or confusion).

Methadone is indicated for use in

- Neuropathic or mixed nociceptive-neuropathic pain, not responding to other agents e.g. NSAID + opioid +antidepressant/antiepileptic
- Neurotoxicity with morphine (myoclonus, allodynia, hyperalgesia, delirium) where conversion to another opioid is not possible
- End stage renal failure[3]

METHADONE continued

Methadone has a complex pharmacodynamics and pharmacokinetic profile, with individual variation in metabolism, and a widely variable plasma half-life (range 5 to 130 hours). Its high volume of distribution and protein-binding contribute to the long plasma half-life, with the risk of accumulation. As it takes 4 to 7 days to reach steady state, dose adjustments are not undertaken less than weekly.

QT interval prolongation has been observed with methadone, generally at higher doses. Caution is required when co-administering methadone with drugs that may prolong the QT, for example, haloperidol, domperidone, ondansetron and citalopram.[3]

Clinically important drug interactions need to be considered when prescribing, as methadone is metabolised in the liver by many of the CYP450 enzymes. Methadone metabolism is increased by carbamazepine, phenobarbital, phenytoin, rifampicin and St John's Wort and may result in a decrease in pain control or withdrawal symptoms. A decrease in methadone metabolism with increase in toxicity can occur with the co-administration of drugs which inhibit CYP450 enzymes, for example, SSRIs, ciprofloxacin and fluconazole.[3]

In clinical practice in Australia, variation in practice in converting to methadone has been reported.[6] Protocols similar to the Palliative Care Formulary[3] use of methadone in cancer pain prescribing guide, are in use in Australia.[15,16] The eventual methadone dose is generally 5 to 10 times smaller than the morphine dose, but may be 20 to 30 times smaller.

The breakthrough dose of methadone is 1/6 to1/10th of the 24 hour methadone dose, and is prescribed every 3 hours when necessary. If more than 2 breakthrough doses are required per day, the regular methadone dose can be increased under the direction of the specialist.
Other opioids can be prescribed for breakthrough dosing if there are concerns about accumulation and toxicity due to frequent breakthrough dosing.

ORAL METHADONE TO SUBCUTANEOUS METHADONE – same drug to same drug

Oral	Subcutaneous	Conversion Ratio	Example	Reference
Methadone	Methadone	1:1 to 2:1	Oral Methadone 20mg = Subcutaneous Methadone 10 to 20mg	3

A 2015 systematic review concluded that while some methods of conversion of strong opioids to methadone appear effective evidence is low. Close monitoring, preferably in the inpatient setting, should be undertaken due to the high risk of adverse effects, with specialist advice; particularly for the frail patient, and those on a high opioid equivalent dose. Adverse effects reported included sedation, respiratory depression and prolonged QT interval.[17]
Methadone conversion to other opioids is infrequently undertaken, with a wide variation in ratio reported.[18]

REFERENCES 2016

1. Fine PG, Portenoy RK. Establishing best practices for opioid rotation; conclusions of an expert panel. J Pain Symptom Manage 2009;38:426-439
2. Smith H S, Peppin J F. Towards a systematic approach to opioid rotation. J Pain Res 2014;7:589-608
3. Twycross R, Wilcock A. Palliative Care Formulary. PDF version, PCF5+, September 2015. Nottingham. Palliativedrugs.com Ltd; 2015
4. Palliative Care Expert Group, Therapeutic Guidelines: Palliative Care.2010 Version 3. Therapeutic Guidelines Limited: Melbourne
5. Mercadante S, Caraceni A. Conversion ratios for opioid switching in the treatment of cancer pain: a systematic review. Palliat Med 2011;25:504-515
6. Syrmis W, Good P, Wootton J, Spurling G. Opioid conversion ratios used in palliative care: is there an Australian consensus? Intern Med J 2014;44:483-489.
7. Targin® product information available at https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2012-PI-01399-3&d=2016011316114622412
8. Galvez R, Schafer M, Hans G, Falke D, Steigerwad I. Tapentadol prolonged release versus strong opioids for severe, chronic low back pain; results of an open label phase 3 study. Adv Ther 2013;30:229-259.
9. Mercandante S, Porzio G, Aielli F, Adile C, Verna L, Ficorella C, Giarrantano A, Casuccio A. Opioid switching from and to tapentadol extended release in cancer patients: conversion ratio with other opioids. Curr Res Med Opin 2013;29:661-666
10. McPherson MM Demystifying opioid conversions: a guide for effective dosing, Bethesda:ASHP;2010
11. White C, Hardy J, Boyd A, Hall A. Subcutaneous sufentanil for palliative care patients in a hospital setting. Palliat Med 2008;22:89-90
12. Reddy A, Tayjasanant S, Haider A, Heung Y, Wu J, Liu D et al. The opioid rotation ratio of strong opioids to transdermal fentanyl in cancer patients. Cancer 2016;122: 149–156
13. Samala RV, Bloise R, Davis M. Efficacy and safety of a six-hour continuous overlap method for converting intravenous to transdermal fentanyl in cancer pain. J Pain Symptom Manage 2014;48:132-146
14. Prommer E. The role of fentanyl in cancer – related pain. J Palliat Med 2009;12:947-54
15. An email (P Tuffin, personal communication, November 5th 2015) regarding the current Methadone Conversion Regimen Royal Perth Hospital
16. An email (M Benson, personal communication, November 6th 2015) regarding the Peninsula Health Clinical Practice Guideline Methadone for Cancer Pain (RoMANCCC)
17. McLean S, Twomey F. Methods of rotation from another strong opioid to methadone for the management of cancer pain: a systematic review of the available evidence. J Pain Symptom Manage 2015;50:248-259.
18. Walker PW, Palla S, Pei B-L, Kaur G, Shang K, Hanohano J, Munsell M, Bruera E. Switching from Methadone to a Different Opioid: What Is the Equianalgesic Dose Ratio? J Palliat Med 2008;11:1103-1108.

Eastern Metropolitan Region
Palliative Care Consortium

Opioid Conversion Ratios - Guide to Palliative Care Practice 2016 Summary Chart

The entire document must be viewed at www.emrpcc.org.au

ORAL MORPHINE TO OTHER ORAL OPIOIDS			
Oral to Oral	**Conversion Ratio**	**Example**	**Comments**
Morphine to Codeine	1:10	Oral Morphine 6mg = Oral Codeine 60mg	**Avoid conversion and treat as opioid naive** Codeine has a limited role in managing moderate-severe pain in palliative care
Morphine to Hydromorphone	5:1	Oral Morphine 5mg = Oral Hydromorphone 1mg	
Morphine to Methadone	**Palliative Care Specialist input required**		
Morphine to Oxycodone	1.5:1	Oral Morphine 15mg = Oral Oxycodone 10mg	The oxycodone component of Targin ® should be considered in conversions
Morphine to Tapentadol	1:3	Oral Morphine 100mg = Oral Tapentadol 300mg	
Morphine to Tramadol	1:5 to 1:10	Oral Morphine 10mg = Oral Tramadol 50 to 100mg	Tramadol has a limited role in managing moderate to severe pain in palliative care

ORAL OPIOIDS TO SUBCUTANEOUS OPIOIDS– same drug to same drug			
Oral	**Subcutaneous**	**Conversion Ratio**	**Example**
Morphine	Morphine	2:1 to 3:1	Oral Morphine 30mg = Subcutaneous Morphine 10 to 15mg
Oxycodone	Oxycodone	1.5:1 to 2:1	Oral Oxycodone 30mg = Subcutaneous Oxycodone 15 to 20mg
Hydromorphone	Hydromorphone	2:1 to 3:1	Oral Hydromorphone 15mg = Subcutaneous Hydromorphone 5 to 7.5mg

SUBCUTANEOUS MORPHINE TO OTHER SUBCUTANEOUS OPIOIDS				
Subcutaneous	**Subcutaneous**	**Conversion Ratio**	**Example**	**Comments**
Morphine	Fentanyl	100:1	Subcutaneous Morphine 10,000micrograms (10mg) = Subcutaneous Fentanyl 100 micrograms	The 100:1 conversion ratio is conservative
Morphine	Hydromorphone	5:1	Subcutaneous Morphine 10mg = Subcutaneous Hydromorphone 2mg	
Morphine	Oxycodone	1:1	Subcutaneous Morphine 10mg = Subcutaneous Oxycodone 10mg	
Morphine	Sufentanil	1000:1	Subcutaneous Morphine 10,000microgram (10mg) = Subcutaneous Fentanyl 100 micrograms = Subcutaneous Sufentanil 10micrograms	Convert to fentanyl initially

MORPHINE TO TRANSDERMAL FENTANYL			
Oral Morphine (mg/24 hours)	**Subcutaneous Morphine (mg/24 hrs) (Dose ratio 3:1 to 2:1)**	**Transdermal Fentanyl (mcg/24 hours) (Dose ratio from oral morphine 100:1)**	**Transdermal Fentanyl (mcg/ hour) Patch Size**
30	10 to 15	300	12
60	20 to 30	600	25
120	40 to 60	1200	50
180	60 to 90	1800	75
240	80 to 120	2400	100
Seek specialist palliative care advice when converting at high doses			

TRANSDERMAL BUPRENORPHINE TO ORAL MORPHINE				
Patch Strength	**Delivery Rate**	**Conversion Ratio**	**Calculation**	**Comments**
Buprenorphine **5 mg/7 days** (120micrograms /24 hours)	5 micrograms / hour	1: 75 – 1:100	5mg patch = 5micrograms buprenorphine per hour 5microgram x 24 = 120micrograms over 24 hours 120microgram buprenorphine x 75 = 9,000microgram (9 mg) or x 100 = 12,000 microgram (12mg) of oral morphine	Oral Morphine dose 9 to 12mg/24 hours
Buprenorphine **10 mg/7 days** (240micrograms /24 hours)	10 micrograms / hour	1: 75 – 1:100	10mg patch = 10 micrograms buprenorphine per hour 10microgram x 24 = 240micrograms over 24 hours 240microgram buprenorphine x 75 = 18,000microgram (18mg) or x 100 = 24,000microgram (24 mg) of oral morphine	Oral Morphine dose 18 to 24mg/24 hours
Buprenorphine **20 mg/7 days** (480micrograms /24 hours)	20 micrograms / hour	1: 75 – 1:100	20mg patch = 20micrograms buprenorphine per hour 20microgram x 24 = 480 micrograms over 24 hours 480 micrograms buprenorphine x 75 = 36,000micrograms (36mg) or x 100 = 48,000micrograms (48mg) of oral morphine	Oral Morphine dose 36 to 48mg/24 hours. Maximum transdermal dose recommended is 40microgram/hour (2 x 20mg/7day patches)
Breakthrough pain is treated with immediate release opioid e.g. morphine or oxycodone. On removal of the buprenorphine patch, a short acting opioid should be prescribed for the initial 24 hours and a long acting opioid commenced after 24hours				

The information in this summary is to be read in conjunction with the entire document. It is the responsibility of the user to ensure the information is used correctly. This guide reflects current palliative care practice in the Eastern Metropolitan Region of Melbourne and published evidence at the time of the release.
All medication doses should be checked and prescribed by a medical doctor or nurse practitioner with appropriate experience in opioid prescribing.
Medication doses should be modified in response to the patient/client's clinical situation and status, including previous exposure to opioids and concurrent medications. All patients should be monitored closely until stable when commencing, adjusting dosage and/or switching opioid medications.
Adhere to all legislation and professional requirements including organisational policies and procedures regarding opioid medications and their administration.