Q&A 42.8

What are the equivalent doses of oral morphine to other oral opioids when used as analgesics in adult palliative care?

Prepared by UK Medicines Information (UKMi) pharmacists for NHS healthcare professionals
Before using this Q&A, read the disclaimer at https://www.sps.nhs.uk/articles/about-ukmi-medicines-qas/
Date prepared: 26th September 2016

Background

Morphine is generally the strong opioid of choice for treating moderate to severe cancer pain (1) and a common question is how to convert a dose of another opioid to morphine or vice versa. Other opioids may be preferred, for example, if a patient obtains insufficient pain relief with morphine (or other strong opioid) and/or is suffering severe adverse effects (1,2,3). However, switching to an alternative opioid is only one approach to managing opioid adverse effects. Other strategies include (2):

- Reducing the dose of opioid (and possibly adding adjuvant analgesics).
- Symptomatic management of the adverse effect(s).
- Switching the route of administration.

If the strategies above have not worked, or are impractical, then a decision to convert to an alternative opioid may be taken, preferably with advice from a palliative care or pain team.

Answer

Advice on opioid conversion

NB: Before using Table 1, read the notes below and the Limitations statement at the end of this document.

- Equivalent doses of opioids are given in Table 1. These are an **approximate** guide only because comprehensive data are lacking and there is inter-individual variation (3). In addition, it should be noted that sources differ in the equivalent doses they quote. Caution is required and careful monitoring during conversion is necessary to avoid both underdosing and excessive dosing (3).

- When converting from one opioid to oral morphine, or vice versa, the initial dose depends on the relative potency of the two drugs (2,3) and route of administration (2). **This Q&A deals only with oral administration (see Table 1).**

- Some authors have suggested that, in most cases, the calculated dose-equivalent of a new drug derived from e.g. Table 1 must be reduced to ensure safety. Based on clinical experience and published guidelines, the starting point for dose reduction from the calculated equianalgesic dose is 25-50% (2,4,5). This dose reduction is particularly important when high doses are used (4). However, the reduction may not be appropriate if the original opioid failed to control pain (see below). Reasons for this suggested dose reduction include:

    - Incomplete cross-tolerance between opioid drugs. This refers to how the tolerance to an opioid currently administered to a patient may not extend to an equivalent dose of another opioid.

This may lead to effects (including adverse effects) that would be greater than expected based on equivalent dosing when a switch to a new drug is made (2).

- There appears to be a large inter-individual variability in response (2).
- There is a need to adjust for conditions that increase opioid risk (e.g. elderly patients, co-existing medical conditions) (4).
- Most published opioid conversion tables have been derived from short-term studies in opioid-naive patients, which do not account for the influence of incomplete cross-tolerance between opioids (2).

- A dose reduction of at least 50% is recommended when switching at high doses (e.g. morphine or equivalent doses of 1g/24 hours or more), in elderly or frail patients, or because of intolerable undesirable effects (3). A similar dose reduction is recommended when there has been a recent rapid escalation of the first opioid. 'As required' doses should be used to make up any deficit while re-titrating to a satisfactory dose of the new opioid (3).

- When considering opioid conversions, the severity of the pain should also be taken into account. For example, if pain is not controlled by the current opioid then it may be appropriate to administer the calculated equianalgesic dose of the new opioid (4).

- The half-life of the two drugs needs to be considered when converting so that the patient does not experience breakthrough pain or receive too much opioid during the conversion period.

- The time to onset of action needs to be considered, for example, if moving from a non-modified release to a modified release preparation. The timing of doses will therefore need to be carefully considered.

- The total daily dose of the current opioid(s), including all long-acting and breakthrough doses, must be determined prior to conversion. If the patient is on multiple opioids, convert all to morphine equivalents (see Table 1) (2).

- Ensure that 'as required' doses of an opioid are prescribed for breakthrough pain (2,6). These should **not** be modified release preparations or transdermal patches.

- Once the conversion has occurred, the dose of new opioid should be titrated carefully according to individual response (1,4) and the patient monitored closely for side effects and efficacy, especially when switching at high doses (6). Careful monitoring is also particularly necessary when there has been a recent rapid escalation of the first opioid (6). In selected patients who do not obtain a satisfactory therapeutic outcome (improved pain relief or fewer adverse effects), further conversion to a different opioid may be required (2,4).

- Ensure naloxone is available.

Table 1. Approximate equivalent potencies of oral opioids to oral morphine (see advice above).

Converting from another oral opioid to oral morphine: **Multiply** the total daily dose of oral opioid by its potency equivalence to determine the equivalent total daily dose of oral morphine.
Converting from oral morphine to another oral opioid: **Divide** the total daily dose of oral morphine by the potency equivalence for the oral opioid which you are converting to.

Oral Drug (refs)	**Duration of action** (hours) (standard release preparations)	**Potency equivalence to morphine** (oral to oral)	**Notes**
Buprenorphine (7,8)	6 - 8	80 (sublingual)	Care required as only one literature source suggests a conversion (7) although this potency equivalence has been cited for a number of years. No dose equivalence studies comparing sublingual buprenorphine with oral morphine have been published (8). Reports of undesirable effects in patients switched to high doses of buprenorphine (6-24mg/24h) (7).
Codeine (3,9-13)	3 – 6	0.08 - 0.1	Codeine is partly metabolised to morphine (10).
Dihydrocodeine (3,9,12-14)	3 - 6	0.1	
Hydromorphone (1,3,6,11-13,15,16)	4 - 5	3.5 - 10	Some sources suggest using a potency equivalence of 5 when converting from morphine to hydromorphone (15). The manufacturer states an approximate potency equivalence of 5-10 (16).
Morphine (3,17)	3 - 6	1	
Oxycodone (1,3,11-13,18-21)	3 - 6	1.5 - 2	Note high oral bioavailability compared to morphine (18,19). One manufacturer advises a potency equivalence of 1.5 - 2 with prolonged release formulations, together with a 25-50% dose reduction following conversion (20). Other manufacturers state an approximate potency equivalence of 2 (19,21).
Tapentadol (3,22,23)	4-6	0.3 - 0.8	Manufacturer states that direct opioid conversion has not been studied so potency equivalence has been calculated indirectly. Manufacturer suggests an analgesic potency equivalence of 0.4 - 0.8 (23). Switching from another μ agonist (e.g. morphine) may cause low-grade opioid withdrawal and as required doses of the original opioid should be used to counter this. Role of tapentadol in palliative care is unclear (3).
Tramadol (3,11,13,24,25)	3 – 9	0.1 - 0.17	Manufacturer advises a potency equivalence of 0.1 - 0.17 (25).

Equivalent potencies are only approximate and can be unpredictable. When converting from one opioid to another, it is often appropriate to use a lower dose than the suggested equivalence above. Close monitoring for side effects and efficacy is mandatory, especially at higher doses.

Example conversion:

Converting from morphine m/r 15mg bd to oral oxycodone:

- Total daily dose of morphine is 30mg.
- From Table 1, oxycodone potency equivalence = 1.5 – 2.
- Divide 30mg/1.5 = 20mg and 30mg/2 = 15mg.
- Therefore the approximate equivalent total daily dose of oral oxycodone is 15 - 20mg in divided doses. See notes above on how this should be used in practice.

Limitations

- Evidence for the effectiveness of switching opioids when managing cancer pain or chronic non-cancer pain is limited (1,4,26).
- Considerable inter-individual differences exist in the pharmacokinetic and pharmacodynamic behaviour of different opioids, so individual dose titration is essential (26).
- Much of the dose equivalence information was derived from short term trials conducted in patients with acute post-operative pain, or patients with cancer pain on low-dose opioids and therefore may have limitations in applicability to repetitive administration and/or relatively high doses (4).
- The studies that are available have differing patient populations, study methods and small sample sizes. The duration of opioid exposure and the issue of tolerance are also factors in the interpretation of data (27).
- It has been suggested that the directional quality of cross tolerance may not be equal and has not been fully explored. Ratios may change according to the direction of an opioid switch; however the clinical relevance of this is not clear (27,28). Although it is unlikely to have a major impact when switching at lower doses, it is possible that failure to recognise the directional difference may result in negative consequences when switching at higher doses (28).
- Dose conversion tables are not meant to provide recommended initiation doses for a given opioid or patient (29).
- Further trials are needed to optimise conversion ratios when switching from one opioid to another (26).
- The data presented are derived from adults and so may not be applicable to children.
- Published data on opioid substitution therapy and combination preparations have been excluded.

References

1. Caraceni A, Hanks G, Kaasa S et al for the European Palliative Care Research Collaborative (EPCRC), on behalf of the European Association for Palliative Care (EAPC). Use of opioid analgesics in the treatment of cancer pain: evidence-based recommendations from the EAPC. Lancet Oncol 2012;13:e58-68.
2. Slatkin NE. Opioid switching and rotation in primary care: implementation and clinical utility. Curr Med Res Opin 2009;25(9);2133-2150.
3. Twycross R, Wilcock A (eds).Strong opioids monograph. Updated August 2016. Palliative Care Formulary. Accessed via http://www.palliativedrugs.com/ on 21st September 2016
4. Fine PG, Portenoy RK. Establishing “best practices” for opioid rotation: conclusions of an expert panel. J Pain Symptom Manage 2009;38(3):418-425.
5. Nuckols TK, Anderson L, Popescu I et al. Opioid prescribing: A systematic review and critical appraisal of guidelines for chronic pain. Ann Intern Med 2014;160:38-47.
6. Twycross R, Wilcock A (eds). Opioid dose conversion ratios monograph. Updated August 2016. Palliative Care Formulary. Accessed via http://www.palliativedrugs.com/ on 21st September 2016.

7. Twycross R, Wilcock A (eds). Buprenorphine monograph. Updated August 2016. Palliative Care Formulary. Accessed via http://www.palliativedrugs.com/ on 21st September 2016.
8. Personal communication Medical Information Professional Information Ltd on behalf of Indivior Ltd. 26th September 2016.
9. Twycross R, Wilcock A (eds). Weak opioids monograph. Updated August 2016. Palliative Care Formulary. Accessed via http://www.palliativedrugs.com/ on 21st September 2016.
10. Twycross R, Wilcock A (eds). Codeine phosphate monograph. Updated August 2016. Palliative Care Formulary. Accessed via http://www.palliativedrugs.com/ on 21st September 2016.
11. Wessex and ASWCS Palliative Physicians. The Palliative Care Handbook. Advice on clinical management. 8th Edition. 2014 Accessed online via http://www.southernhealth.nhs.uk/ on 21st September 2016
12. Regnard C, Dean M (eds). A Guide to Symptom Relief in Palliative Care 6th edition. Radcliffe Publishing. Oxford; 2010:67.
13. Pain management with opioids. Joint Formulary Committee. British National Formulary. London: BMJ Group and Pharmaceutical Press. Accessed via www.medicinescomplete.com on 21st September 2016
14. Twycross R, Wilcock A (eds). Dihydrocodeine tartrate monograph. Updated August 2016 Palliative Care Formulary. Accessed via http://www.palliativedrugs.com/ on 21st September 2016
15. Twycross R, Wilcock A (eds). Hydromorphone monograph. Updated August 2016. Palliative Care Formulary. Accessed via http://www.palliativedrugs.com/ on 21st September 2016.
16. SPC Palladone (hydromorphone) capsules. Napp Pharmaceuticals Ltd. Accessed via http://www.medicines.org.uk/emc/ on 21st September 2016 (SPC last updated on the eMC: 24th September 2014).
17. Twycross R, Wilcock A (eds). Morphine monograph. Updated August 2016. Palliative Care Formulary. Accessed via http://www.palliativedrugs.com/ on 21st September 2016.
18. Twycross R, Wilcock A (eds). Oxycodone monograph. Updated August 2016. Palliative Care Formulary. Accessed via http://www.palliativedrugs.com/ on 21st September 2016.
19. SPC OxyNorm (oxycodone) 5, 10, 20mg. Napp Pharmaceuticals Ltd. Accessed via http://www.medicines.org.uk/emc/ on 21st September 2016 (SPC last updated on the eMC: 14th August 2015).
20. SPC Dolocodon (oxycodone) PR 10mg prolonged release tablets. Zentiva. Accessed via http://www.mhra.gov.uk/spc-pil/ on 22nd September 2016 (SPC last updated on the 28th March 2014).
21. SPC Longtec 5mg, 10mg, 15mg, 20mg, 30mg, 40mg, 60mg, 80mg and 120mg prolonged release tablets. Qdem Pharmaceuticals Ltd. Accessed via http://www.medicines.org.uk/emc/ on 22nd September 2016 (SPC last updated on the eMC: 15th August 2016).
22. Twycross R, Wilcox A (eds) Tapentadol monograph. Updated August 2016. Palliative Care Formulary. Accessed via http://www.palliativedrugs.com/
23. Personal communication, Medical Information department Grünenthal Ltd. 22nd September 2016.
24. Twycross R, Wilcock A (eds). Tramadol monograph. Updated August 2016. Palliative Care Formulary. Accessed via http://www.palliativedrugs.com/ on 22nd September 2016.
25. SPC Zydol 50mg capsules. Grünenthal Ltd. Accessed via http://www.medicines.org.uk/emc/ on 22nd September 2016 (SPC last updated on the eMC: 12th Feb 2015).
26. Vissers KCP, Besse K, Hans G et al. Opioid rotation in the management of chronic pain: where is the evidence? Pain Practice 2010;10(2):85-93.
27. Berdine HJ, Nesbit SA. Equianalgesic dosing of opioids. J Pain Palliat Care Pharmacother 2006;20:79-84.
28. Pereira J, Lawlor P, Vigano A et al. Equianalgesic dose ratios for opioids: a critical review and proposals for long-term dosing. J Pain Symptom Manage 2001;22:672-687.
29. Anderson R, Saiers JH, Abram S et al. Accuracy in equianalgesic dosing: conversion dilemmas. J Pain Symptom Manage 2001;21:397-406.

Quality Assurance

Prepared by
Joshua McKie, Lead Pharmacist Critical Evaluation (based on earlier work by Kate Pickett, Louisa Rowlands and Anne Cole), Southampton Medicines Advice Service, University Hospital Southampton NHS Foundation Trust.

Date Prepared
26th September 2016

Contact:
medicinesadvice@uhs.nhs.uk

Checked by
Samantha Owen, Principal Pharmacist Critical Evaluation, Southampton Medicines Advice Service, University Hospital Southampton NHS Foundation Trust.

Date of check
7th October 2016

Search strategy

- Embase - search strategy: "opioid.af AND equivalence.af"
  "(exp opiate agonist/ OR exp narcotic analgesic agent/ OR exp narcotic agent/) AND equivalence.af (limited to H=Y and LG=EN)"
  "(exp opiate agonist/ OR exp narcotic analgesic agent/ OR exp narcotic agent/) AND exp bioequivalence/ (limited to H=Y and LG=EN)"

- Medline - search strategy: "opioid.af AND equivalence.af"
  "(exp analgesics, opioid/ OR exp narcotics/) AND exp therapeutic equivalency/ (limited to H=Y and LG=EN)"

- Palliative Care Formulary. Accessed via http://www.palliativedrugs.com/
- Electronic Medicines Compendium. Accessed via / http://www.medicines.org.uk/emc/
- NICE. Accessed via www.nice.org.uk
- Palliative Care Guidelines Plus. Accessed via http://book.pallcare.info/
- Cochrane Library. Accessed via http://www.thecochranelibrary.com/
- NICE Evidence. Accessed via www.evidence.nhs.uk
- SIGN Guidelines. Accessed via http://www.sign.ac.uk
- European Association for Palliative Care. Accessed via http://www.eapcnet.eu/
- American Pain Society. Accessed via www.ampainsoc.org
- American College of Physicians. Accessed via www.acponline.org
- Specialist textbooks
- Personal communication Medical Information Reckitt Benckiser (Temgesic). November 2013
- Personal communication Medical Information Indivior (Temgesic) September 2016
- Personal communication Medical Information Grünenthal Ltd (Palexia). September 2016