

# Oxycodone

## – Place in therapy

### Key concepts:

- Oxycodone is a strong opioid and is a second line option (after morphine) for use at step three on the WHO analgesic ladder
- Morphine remains the first-line strong opioid and oxycodone should be reserved for specific situations
- Oxycodone can be considered if morphine is poorly tolerated
- Oxycodone is not a substitute for codeine at step two on the analgesic ladder. If the response to codeine is unsatisfactory, morphine should be considered (i.e. step three)
- Oxycodone has a number of potentially significant drug interactions that do not occur with morphine
- Oxycodone is not completely safe in renal impairment


### Oxycodone use is increasing

The use of oxycodone has been steadily increasing over the last three to four years (Figure 1).

This trend is similar to patterns observed in other countries such as the UK and Australia and corresponds with a prominent marketing campaign suggesting that oxycodone should be the preferred opioid analgesic for the treatment of moderate to severe persistent pain. Oxycodone is more expensive than morphine, has a similar side effect profile and there is no clinical evidence to support its use first-line.

### Oxycodone is a strong opioid similar to morphine

Oxycodone is a semi-synthetic opioid with effects similar to morphine. It is an alternative to morphine for severe pain at step three on the WHO analgesic ladder

 See BPJ 16, September 2008 “Pharmacological management of chronic pain”.

Clinical trials indicate that oxycodone is as effective as morphine at controlling cancer pain but with no significant difference in overall tolerability. There is no evidence that oxycodone is superior to morphine for chronic, non-cancer pain.

There is some evidence that there is individual variation in analgesic response and sensitivity to the adverse effects of opioids.<sup>1</sup> Oxycodone can be considered for the small number of patients who experience allergy or ongoing neurotoxic adverse effects to morphine, such as hallucinations. Oxycodone may have a place in the management of complex pain syndromes.

### **Oxycodone is not a substitute for codeine at step two on the analgesic ladder**

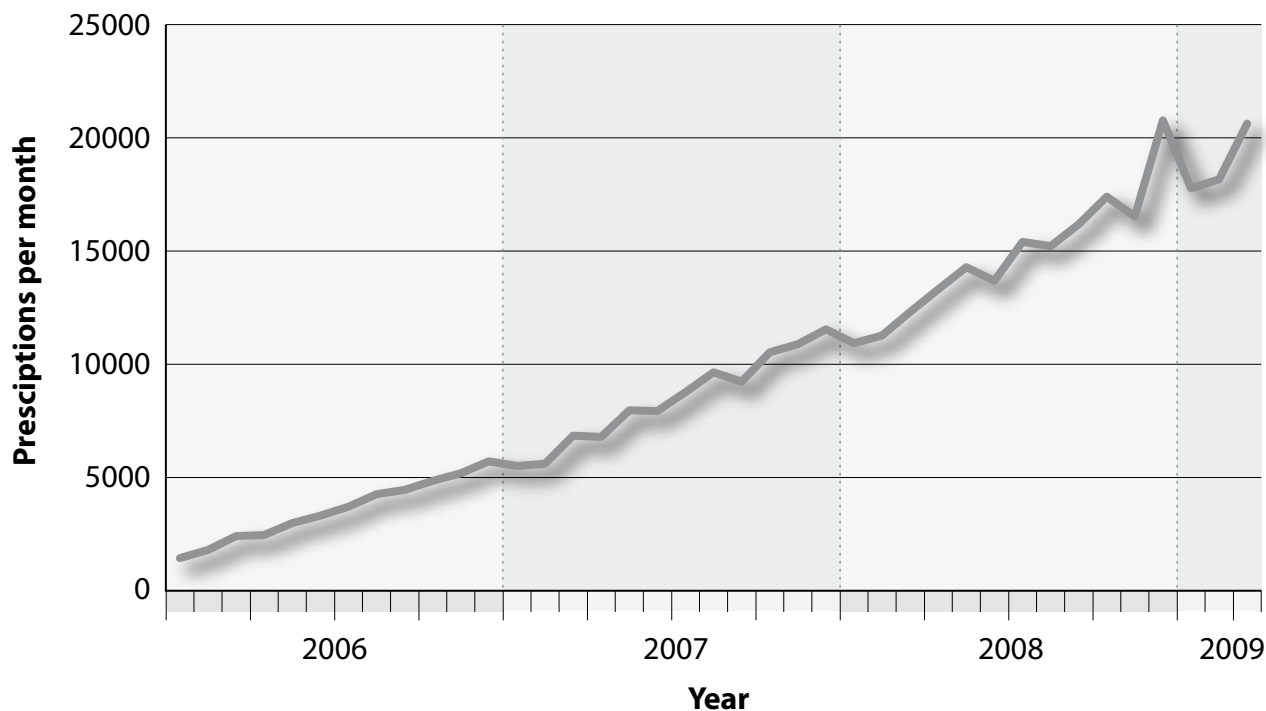
One possible reason for the increased prescribing of oxycodone is that it is being used in place of codeine. From its name (oxycodone) it may be perceived as being

similar to codeine (a weak opioid), but in fact oxycodone is a strong opioid twice as potent as morphine and with similar adverse effects. If pain is not controlled adequately with a step two analgesic, including codeine, progress to step three might be indicated with morphine as the first line choice.

### **Precautions**

#### **Potential drug interactions**

Oxycodone shares the same drug interactions as the other opioid analgesics. However, in contrast to morphine, the enzymes CYP2D6 and CYP3A4 are involved in the hepatic metabolism of oxycodone, and there is the potential for drugs which inhibit these enzymes (e.g. fluoxetine, erythromycin) to increase oxycodone plasma concentrations. There appears to be little evidence at present that these potential interactions are clinically significant, but as with any drug it is important to check the interaction profile prior to prescribing.



**Figure 1:** Number of oxycodone prescriptions in New Zealand 2006 to 2009 (Pharmaceutical Warehouse data)

## Promotion of oxycodone

Oxycodone preparations have been heavily marketed over the last few years but advertisements do not provide useful information to guide its rational and appropriate use.

- The wording in the advertisements strongly suggests to the prescriber that oxycodone is generally superior to other opioid analgesics, but does not provide any evidence to support this.
- All statements supporting the use of oxycodone could be equally applied to morphine.
- When the trials that are cited to support the efficacy of oxycodone are analysed, it is found that they do not describe any benefits over other opioid analgesics. For example, the statement “proven efficacy in providing long acting relief from moderate to severe persistent pain” is supported by three references:
  - A comparison between modified release and normal release oxycodone for chronic back pain (equally effective)<sup>2</sup>
  - A controlled trial of oxycodone versus placebo for osteoarthritis pain (oxycodone superior to placebo)<sup>3</sup>
  - A comparison of controlled release morphine with controlled release oxycodone in cancer pain (equally effective)<sup>4</sup>
- None of these trials indicate that oxycodone is anything other than an effective second-line alternative to morphine.

## Adverse effects

Oxycodone is not a safer alternative to other opioid analgesics and it has the same spectrum of adverse effects. Of greatest concern is the potential for respiratory depression when used at too high a dose or when combined with other CNS depressants such as benzodiazepines and alcohol. Combination with other opioids is potentially lethal and care should be taken to avoid this, especially if people might have access to a supply of both, e.g. after switching from morphine.

## Dosage adjustment still required in renal impairment

Oxycodone has a better profile in renal impairment as, unlike morphine, it does not have active metabolites that are renally excreted. However, caution is still required as the half-life of oxycodone is increased with renal impairment and dosage adjustment is required.

## Prescribing oxycodone

The pharmacodynamics of morphine and oxycodone are comparable and equivalent formulations can be used in similar ways. Oxycodone is available as:

- OxyNorm = normal release liquid (5 mg/5 mL) and capsules (5 mg/10 mg/20 mg)
- OxyContin = modified release tablets (5 mg/10 mg/20 mg/40 mg/80 mg). The modified release tablets have a biphasic release profile, which gives an onset of analgesia within an hour of dosing and a duration of action of 12 hours
- Parenteral formulation (OxyNorm 10 mg/mL) for subcutaneous or intravenous injection or infusion. This is 1.5 to 2 times more potent than oral oxycodone.

## Changing from oral morphine

Oral oxycodone is approximately twice as potent as oral morphine. To convert from oral morphine to oxycodone it is necessary to halve the dose e.g. 10 mg morphine is equivalent to 5 mg of oxycodone. It is important to note

that conversion rates are an approximate guide and patient response should be carefully monitored.

### Starting oxycodone in an opioid naïve patient

It is uncommon to commence oxycodone in an “opioid naïve” patient. One reason to consider this would be in a “morphine phobic” patient who can be convinced to trial an opioid with a different name.

If opioid treatment with oxycodone is commenced, one possible approach is:

1. Start with normal release formulation to find the daily dose required. As the half-life of the OxyNorm is slightly longer than the half-life of morphine it may be dosed at six hourly rather than four hourly intervals.

Example of a prescription for an “opioid naïve” patient with normal renal function:

Oxynorm 2.5 mg to 5 mg four to six hourly

#### Plus

**A = antiemetic** e.g. haloperidol 1.5 mg nocte or as required for first five to seven days

**B = breakthrough** Calculate the “as required” dose (prn) at 1/6th to 1/10th of the 24 hour regular prescription. For example if taking Oxynorm 2.5 mg four hourly (= 24 hour dose of 15 mg), prescribe prn dose of 2.5 mg (maximum one extra dose, two hourly)

**C = constipation** Start regular laxatives e.g. Laxsol one to two tablets twice daily and alter the dose depending on effect

2. Titrate up. If requiring extra doses, or in pain, increase the regular and the prn dose by 30–50% by going from 2.5 mg to 5 mg, to 7.5 mg, to 10 mg, to 15 mg, to 20 mg, to 30 mg, to 40 mg etc.
3. Once the dose is stable, and the pain controlled, add up all the doses required in a 24 hour period (regular and prn) and divide by two to find the modified release twice daily dose.

For example Oxynorm 10 mg, six doses each day, which adds up to 60 mg, is equivalent to Oxycontin 30 mg twice daily.

Reassess:

**A** – Any nausea should be settled by the first week.

**B** – Always prescribe equivalent breakthrough e.g. if taking Oxycontin 30 mg twice daily, prescribe Oxynorm 5 mg to 10 mg prn (maximum one extra dose, two hourly)

**C** – Remember to reassess bowel function and readjust laxative dose as appropriate

An alternative approach is to start with a low dose of modified release oxycodone (Oxycontin). This may be particularly appropriate for benign chronic pain where the goal is not complete pain control but improvement in function. For example, start with 5 mg every 12 hours. The dose can then be titrated to effect as necessary.

### Key resource:

Christchurch Hospital Palliative Care Service. Palliative Care Guidelines. Canterbury District Health Board, 2009. Available from: [www.cdhb.govt.nz/documents/palliative-care-manual/palliative-care/Pal\\_Care\\_Guidelines.pdf](http://www.cdhb.govt.nz/documents/palliative-care-manual/palliative-care/Pal_Care_Guidelines.pdf) (Accessed September 2009).

### References

1. Cherny N, Ripamonto C, Pereira J, et al. Strategies to manage the adverse effects of oral morphine: an evidence based report. *J Clin Oncol* 2001;19(9):2542-54.
2. Hale M, Fleischmann R, Salzman R, et al. Efficacy and safety of controlled-release versus immediate-release oxycodone: randomized, double-blind evaluation in patients with chronic back pain. *Clin J Pain* 1999;15(3):179-83.
3. Roth S, Fleischmann R, Burch F, et al. Around-the-clock, controlled-release oxycodone therapy for osteoarthritis-related pain. *Arch Intern Med* 2000;160(6):853-60.
4. Mucci-LoRusso P, Berman B, Silberstein P, et al. Controlled release oxycodone compared with controlled release morphine in the treatment of cancer pain: a randomized, double blind, parallel group study. *Eur J Pain* 1998;2(3):239-49.