Oxycodone

Class
Semi-synthetic strong opioid agonist with affinity for mu and kappa receptors.
Potency ratio; Oral oxycodone is 2 times more potent than oral morphine
  e.g. 10mg oral oxycodone = 20mg oral morphine.

Indications
For use in patients with moderate/severe cancer pain when patients require a strong opiate but have
morphine intolerance (approx 5% of patients with severe cancer pain)

Definition of morphine intolerance
Morphine intolerance is defined as the development of unacceptable side effects from morphine which
prevent an adequate dose of morphine to be administered in a patient with opiate sensitive pain. The
symptoms which would suggest morphine intolerance are hallucinations, confusion, cognitive
impairment, marked sedation, pruritus and intractable vomiting, brought on by starting morphine or
increasing the dose of morphine.

Clinical effect
Oxycodone does not undergo extensive first pass metabolism and therefore has a high
bioavailability (60-87%) This leads to a more predictable pharmacokinetic profile compared with morphine. Oxycodone is
metabolised to oxymorphone and noroxycodone, both of which contribute minimal pharmacological
activity. Once at steady state neither oxycodone nor its metabolites have been shown to accumulate
during repeated oral use.

Preparations
Modified release tablets (OxyContin) 5mg, 10mg, 20mg, 40mg, 80mg
Normal release capsules (OxyNorm) 5mg, 10mg, 20mg
Normal release liquid (OxyNorm) 1mg/ml
Normal release liquid concentrate (OxyNorm) 10mg/ml
OxyNorm solution for injection 10mg/ml

Dosage regimen
Starting oxycodone:
There are two possible regimes.

1. **OxyContin (modified release) tablets** administered every 12hrs.
   The starting dose is dependent on the severity of pain and the patient’s previous analgesic
   requirements. The usual starting dose is 10mg bd for opiate naïve patients or for patients with
   pain uncontrolled by weak opioids. Doses should be titrated in dose increments of 25-50%.
   
   **If converting from oral morphine:**
   - Add up the total 24 hr oral morphine requirement (regular and prn)
   - Divide by 2 to calculate the total 24 hr dose of oxycodone.
   - Divide this dose by 2 and prescribe OxyContin 12 hourly.

   If converting from another opioid use potency ratio to calculate appropriate dose (**see oral opioid
   potency rate protocol**).
Modified release preparations are biphasic i.e. an initial relatively fast release leading to early onset of analgesia and a slow release to provide a 12hr duration of action.

OxyContin tablets must be swallowed whole: taking them crushed or chewed could lead to the rapid release and absorption of a potentially toxic dose of oxycodone.

2. OxyNorm capsules or liquid (normal release) administered q4-6hrly and titrated until pain control is achieved. If a patient is opioid naïve the starting dose would be 2.5mg PO q4-6hr

If converting from oral morphine to oral OxyNorm:
- Add up total 24 hr oral morphine dose (regular and prn)
- Divide by 2 to calculate total 24 hr dose of oxycodone
- Divide this dose by 6 and prescribe as q4hr OxyNorm
- Once pain control is achieved this dose can be converted to modified release Oxycontin. To calculate this: add up the total 24hr dose of OxyNorm and divide by two to give the 12hrly dose of OxyContin.

Breakthrough pain
Normal release oxycodone (OxyNorm) can be used for breakthrough pain. The dose used will be based on 1/6th of the total 24hr dose of Oxycontin.

e.g. A dose of OxyContin 60mg/24hrs would mean a 10mg dose of OxyNorm capsule or liquid for breakthrough pain. This dose can be administered q4-6hrly as required.

If a patient is opioid naïve the starting dose would be 2.5mg OxyNorm PO q4-6hr

Dosage regime in hepatic/renal failure
Oxycodone is contraindicated in patients with moderate to severe hepatic impairment or severe renal impairment (creatinine clearance <15ml/min)

Oxycodone should be used conservatively in patients with mild/moderate hepatic or renal impairment. These patients should be started on OxyContin 5mg bd PO or OxyNorm 2.5mg q6hr PO

Parenteral Oxycodone
OxyNorm solution is available for parenteral use. The conversion ratio for oral: parenteral oxycodone is 2:1

e.g. Total 24 hr dose oral oxycodone = 24 hr dose OxyNorm solution for injection CSCI

If parenteral breakthrough doses are required these should be calculated as 1/6th of the total 24 dose of OxyNorm in the syringe driver

Side effects
For full list see manufacturers SPC
Most commonly presenting side effects are constipation, nausea and vomiting, dizziness, pruritus, urticaria, dry mouth, sweating, drowsiness. There is evidence that the incidence of hallucinations is less frequent than with morphine.

References
- Shamsul S, Hardy J. Oxycodone : a review of the literature. European J of Palliative Care 2001;8(3) 93-96
- Heiskanen T, Kalso E. Controlled release oxycodone and morphine in cancer related pain. Pain 1997; (73) 37-45
• Kaiko R et al. Clinical Pharmacokinetics of controlled release oxycodone in renal impairment. Clinical pharmacology and Therapeutics 1996;59: 130
• Smith M et al. Oxycodone has a distinctly different pharmacology from morphine. European Journal of Pain 2001 15 135-136