Oxycodone - Palliative Care (Adults)

Contents

1. Overview

Purpose

This protocol outlines the administration, prescribing and monitoring of oxycodone used in the palliative care setting at Te Whatu Ora - Waitematā.

Scope

All medical and nursing staff.

⚠ This guideline is for use in the care of Palliative Care patients ONLY.

2. Presentation & Storage

Formulation	Brand Name	Strength
Oxycodone Hydrochloride Ampoules for injection	Oxynorm®	20mg/2mL (=10mg/ml) 50mg/mL (high strength)
Oxycodone Oral Immediate Release Liquid	Oxynorm®	5mg/5ml (= 1mg/ml)
Oxycodone Oral Immediate Release Capsules	Oxynorm®	5mg, 10mg, 20mg
Oxycodone Oral Controlled Release/Modified Release Tablets	Oxycodone Sandoz®	5mg, 10mg, 20mg, 40mg, 80mg
Note: Immediate Release = short acting Controlled Release/Modified Release = long acting		

Store at room temperature below 25°C. Protect from light.
Medications either stored in Pyxis machine or controlled drug safe.

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3. Indications

Licensed:

- Moderate to severe pain which is opioid responsive
- Oral, subcutaneous and intravenous administration.[1]

Note: Oxycodone is more expensive than morphine and should generally be reserved for patients who cannot tolerate morphine.[2]

4. Contraindications and Precautions

Contraindications:

- Hypersensitivity to oxycodone or any of the constituents of the subcutaneous preparation
- Severe hepatic impairment
- Severe renal impairment (creatinine clearance < 10ml/min)
- Paralytic ileus
- Acute severe airway disease
- Patients on monoamine oxidase inhibitors (MAOIs) or within the previous 14 days.[1, 2]

Precautions:

- Respiratory depression
- Raised intracranial pressure
- Renal impairment (creatinine clearance 10-50 ml/min)
- Hepatic impairment
- Severe CNS depression
- Convulsive disorders.[1, 6]

5. Mechanism of Action

Oxycodone is a full opioid agonist with similar properties to morphine. It has affinity for kappa, mu and delta opioid receptors in the brain and spinal cord. It has good oral bioavailability of up to 87% and is metabolised mainly by CYP3A4 enzyme to its inactive metabolite. Up to 20% of oxycodone is excreted unchanged which can accumulate in renal impairment.[1, 5, 7]

6. Dose

Always specify the formulation when prescribing ORAL oxycodone E.g. oxycodone immediate release or oxycodone controlled release/modified release (i.e. DO NOT chart just "oxycodone").

6.1 Introduction

Before prescribing oxycodone, conduct a pain assessment and determine the likely cause of pain so the most effective management can be implemented. Refer to *Te Whatu Ora – Waitematā Pain Assessment – Palliative Care*.

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If the pain is mild to moderate, consider starting with regular non-opioid analgesia (e.g. paracetamol, non-steroidal anti-inflammatory). If the pain is not adequately controlled with these analgesia, or patient has moderate to severe pain, opioids can be considered.
When starting a patient on an opioid, always consider morphine first. Morphine is the gold standard of opioid analgesia; there is significant evidence and experiential base for the use of morphine for moderate to severe pain. Oxycodone should be used first line ONLY if morphine is contraindicated or should be used in caution i.e. true allergy to morphine or renal impairment (creatinine clearance <50ml/min). A systematic review showed no difference in side effect profile between morphine and oxycodone.[3] Refer to *Te Whatu Ora – Waitematā Pain Management – Palliative Care guideline*.

Each patient has a unique sensitivity/response to oxycodone so start with small doses and titrate according to response.

Despite careful titration of oxycodone, some individuals will have intolerable side-effects or a poor analgesic response. If this happens, the following steps should be taken:

1. Review pain diagnosis:
    - Some pains respond poorly to opioids e.g. pain due to spinal cord compression often responds better to high dose dexamethasone.
    - Incident pain may be better treated with another approach.
    - Colicky abdominal pain due to bowel obstruction may be better treated with an antispasmodic e.g. hyoscine butylbromide.
2. Ensure adequate management of side effects:
    - PRN laxatives should be charted (or REGULAR if constipation is a problem).
    - PRN antiemetics should be charted (or REGULAR anti-emetics via a parenteral route if nausea/vomiting is a problem).

⚠ Use a lower dose of oxycodone in frail/elderly patients, opioid naïve patients and in those with severe hepatic impairment or moderate to severe renal impairment. Oral oxycodone is twice as potent as oral morphine (i.e. oral oxycodone 5mg is equivalent to oral morphine 10mg).

6.2 Oral Oxycodone

Starting Dose in Opioid Naïve patients

Generally patients should be prescribed short acting oxycodone initially and converted to controlled/modified release oxycodone after 1-2 days according to patient's opioid requirement.[2]

Oxycodone immediate release

Recommended starting dose:

- **2.5 – 5mg PO q 1 hourly PRN.**

If three or more PRN doses are required in a 24 hour period, consider starting regular oxycodone depending how many doses have been used – see section below under oxycodone controlled/modified release on how to convert from immediate release to controlled/modified release preparation. Also consider re-review of the pain diagnosis.

Oxycodone controlled/modified release

It may be more convenient in some opioid naïve patients to commence regular 12 hourly controlled/ modified release oxycodone at the lowest dose of **5mg PO twice daily.**

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To change from immediate release to controlled/modified release oxycodone preparation (e.g. Oxycodone Sandoz®):

- Calculate the total amount of oxycodone the patient has required over the past 24 hours and divide it by 2 to get the equivalent dose of modified release oxycodone.[2]

e.g. **10mg** immediate release oxycodone over 24 hours = **5 mg BD** controlled/modified release oxycodone.

- Oxycodone controlled/modified release tablets should be charted as a BD dose (q 12 hourly).
- ALWAYS chart PRN doses when charting controlled/modified release oxycodone:
  - PRN doses should be around 1/6th of the total daily dose and charted q 1-2 hourly (e.g. oxycodone immediate release 2.5-5mg PO q 1 hourly PRN).

Increasing Doses of Controlled/Modified Release Oxycodone

- The dose of controlled/modified release oxycodone may need to be increased if more than three PRN doses are needed for breakthrough pain in 24 hours.[2]
- Generally the dose should not be increased more frequently than every 48 hours.
- When the regular controlled/modified release oxycodone dose is increased, the PRN dose should also be increased so it remains about 1/6th of the **total** daily dose of controlled release oxycodone.

Note: If PRN doses are being used predominantly for incident/movement related pain, it may not be necessary to increase the background dose of controlled release oxycodone

Seek advice from the Palliative Care Team or Pain Team if:

- Pain is increasing despite increasing dose of controlled/modified release oxycodone and/or patient is using more than three PRN doses for breakthrough pain per 24 hours

6.3 Subcutaneous Oxycodone

Starting Doses in Opioid Naïve patients

Subcutaneous Bolus Dosing

Start with PRN subcutaneous oxycodone initially – recommended starting dose:

- **2.5mg subcut every 30 minutes PRN**

If more than three PRN doses have been used in a 24 hour period then consider the use of a continuous subcutaneous infusion (CSCI) of oxycodone via a Niki T34 pump.

Continuous Subcutaneous Infusion (CSCI) Dosing

If a patient requires a continuous subcutaneous infusion because of constant moderate to severe pain, consider a starting dose of **5 – 10mg over 24 hours**.

Increasing/Adjusting Dose of CSCI

- Calculate the total amount of oxycodone the patient has required over the past 24 hours (PRN doses and dose given via CSCI if patient was started on this already) and prescribe this amount as a continuous 24 hour infusion. Also chart about 1/6th of the total dose as a PRN dose every 30 minutes for breakthrough pain.
- All continuous subcutaneous infusions should be reviewed at least every 24 hours until pain is stable and only three or fewer PRN doses per 24 hours have been used. If more than three PRN doses have

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been used, consider an increase in the 24 hour infusion by adding the bolus PRN doses given to the existing dose in CSCI. **HOWEVER**, exert caution if more than 6 PRN doses have been used and consider a smaller dose increase of the background 24 hour infusion. (See next point below)

- If the PRN doses have been administered for incident or movement related pain and patient does not have pain at rest, consider an increase in the PRN dose but not the background 24 hour infusion. *Seek advice from the Te Whatu Ora – Waitematā Palliative Care team.*

6.4 Suggested Conversion Ratios

Conversion from one opioid to another is not an exact science. Equianalgesic dose conversion tables have limitations. A major factor is that the oral bioavailability of opioids varies widely and unpredictably between individuals.[2,4]

The conversion table below provides guidance to a safe starting point. Patients should be reviewed 24 hours after conversion from one opioid to another, or from one route to another, and doses adjusted if necessary according to patient requirement.

Medication	Ratio	Example
PO oxycodone : SC oxycodone	2:1	20mg PO oxycodone = 10mg SC oxycodone
SC oxycodone : PO oxycodone	1:1.5*	20mg SC oxycodone = 30mg PO oxycodone
PO morphine : PO oxycodone	2:1**	10mg PO morphine = 5mg PO oxycodone
PO oxycodone : PO morphine	1:1.5**	5mg PO oxycodone = 7.5mg PO morphine
PO morphine : SC oxycodone	2:1	10mg PO morphine = 5mg SC oxycodone
SC morphine : SC oxycodone	1:1	5mg SC morphine = 5mg SC oxycodone
IV oxycodone: SC oxycodone	1:1	5mg IV oxycodone = 5mg SC oxycodone

Note: PO = oral, SC = subcutaneous, IV = intravenous

*When converting from **oral oxycodone** to subcut a ratio of 2:1 should be used, however when converting from subcut to oral oxycodone a ratio of 1:1.5 should be used. ***Each conversion is conservative to account for the wide variability in response to opioids between individuals.***

When converting from **oral morphine to oral oxycodone a conservative conversion ratio of 2:1 should be used. When converting from oral oxycodone to oral morphine a ratio of 1:1.5 should be used. This reduces risk of overdose due to wide variability in systemic bioavailability of oral morphine.

Converting from oral to subcutaneous oxycodone

- If a patient has been taking oral oxycodone but becomes unable to take oral medication for any reason, the dose of oral oxycodone should be converted to a subcutaneous dose.
- Note there is considerable inter-individual variability in the equianalgesic conversion ratio of oxycodone oral to subcut.
- **When converting the patient's usual 24 hour oral dose to a continuous subcutaneous infusion** the safest approach is to convert only the patient's current background dose (don't include PRN doses) by dividing by 2 and then up titrate the next day according to the PRN usage in last 24 hours.

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7. Administration

7.1 Oral

- **Oxycodone controlled release/modified release tablets must NOT be crushed**
- **Oxynorm® capsules** must be swallowed whole. Use Oxynorm® liquid if the patient has difficulty swallowing.

Immediate release oxycodone **should not** be administered at the same time as controlled release oxycodone *unless advised otherwise by the Palliative Care team*. The absorption of oxycodone from Oxycodone Sandoz® tablets is biphasic with 40% of the dose released initially. Onset of analgesia is usually within one hour.[1]

7.2 Subcutaneous

- Oxycodone for injection should be injected through a Saf-T-Intima or directly by a subcutaneous needle
- The Saf-T-Intima should be flushed with 0.2ml of water for injection after administration of medication
- Can be administered via a continuous subcutaneous infusion pump (Niki T34).

Diluent

- For subcutaneous bolus administration oxycodone does not need to be diluted.[1]
- When added to a syringe driver the recommended diluent is water for injection.

Additional Equipment

- Subcutaneous Saf-T-Intima single lumen [ADM140] (*refer to Te Whatu Ora – Waitematā Policy Palliative Care- Subcutaneous Site Selection, Insertion and Monitoring of BD Saf-T-Intima Cannula*)
- Continuous subcutaneous infusion pump (Niki T34) if required.

Compatibility (for oxycodone for injection)

Compatible with:

- water for injection, 0.9% sodium chloride[1]
- metoclopramide, haloperidol, clonazepam, ketamine, levomepromazine, hyoscine hydrobromide, hyoscine butylbromide, midazolam, octreotide, dexamethasone, ondansetron.[2, 5]

Concentration-dependent compatibility with:

- cyclizine[2, 5]

Do not use if the solution is **cloudy or a precipitate** is present.

8. Observation and Monitoring

- Observe and document patient for respiratory depression every 4 hours
- Monitor and document blood pressure and for orthostatic hypotension
- Monitor for excessive drowsiness
- Monitor for constipation and urinary retention
- Monitor for nausea and vomiting particularly at initiation of oxycodone.

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9. Adverse Effects

- Nausea and vomiting
- Pruritus
- Drowsiness
- Constipation
- Headache
- Hypotension, dizziness
- Dyspnoea
- Respiratory depression
- Confusion, hallucinations
- Disorientation
- Vertigo
- Urinary retention
- Dry mouth
- Euphoria and dysphoria
- Tachycardia
- Dyspepsia
- Anorexia
- Insomnia
- Sweating
- Miosis, visual impairment
- Hypersensitivity/pain at injection site
- Dependence/tolerance[1]

10. Drug Interactions

- Anticholinergic agents – increase risk of anticholinergic adverse effects including severe constipation and urinary retention.
- Additive effects with CNS depressants (e.g. alcohol, other opioids, sedatives and hypnotics, benzodiazepines, tricyclic antidepressants).
- Additive respiratory depression with benzodiazepines and other respiratory depressants.
- CYP3A4 inducers may reduce oxycodone plasma concentration (e.g. rifampicin and carbamazepine).
- CYP3A4 inhibitors may increase oxycodone plasma concentration and enhance its effects (e.g. erythromycin, clarithromycin, fluconazole).
- Monoamine oxidase inhibitors (MAOIs):
    - non-selective MAOIs intensify the effects of opioids which can cause anxiety, confusion and significant respiratory depression
    - do not use oxycodone while on an MAOI or within two weeks of stopping.[1, 6]

11. References

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