NEW ZEALAND DATA SHEET

1. Oxycodone Hydrochloride Tablets, USP (Immediate Release), (Amneal)

Oxycodone Hydrochloride 5 mg Immediate Release Tablets

Oxycodone Hydrochloride 10 mg Immediate Release Tablets

Oxycodone Hydrochloride 20 mg Immediate Release Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Oxycodone Hydrochloride Tablets, USP (Immediate Release), (Amneal) contains oxycodone, an opioid agonist.

Each tablet for oral administration contains 5 mg, 10 mg or 20 mg, of oxycodone hydrochloride, USP.

The 5 mg tablets contain the equivalent of 4.6 mg of oxycodone free base.

The 10 mg tablets contain the equivalent of 9 mg of oxycodone free base.

The 20 mg tablets contain the equivalent of 18 mg of oxycodone free base.

Excipients with known effect

The tablets contain lactose as lactose monohydrate.

Each 5 mg tablet contains 49.5 mg lactose monohydrate.
Each 10 mg tablet contains 44.4 mg lactose monohydrate.
Each 20 mg tablet contains 34.25 mg lactose monohydrate.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

5 mg tablets: white, round, biconvex tablets debossed with “A” on the left and “04” on the right of the score on one side and plain on the other side.

10 mg tablets: pink, round, biconvex tablets debossed with “A” on the left and “48” on the right of the score on one side and plain on the other side.

20 mg tablets: grey, round, biconvex tablets debossed with “A” on the left and “50” on the right of the score on one side and plain on the other side.

The tablet can be divided into equal doses.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

The management of opioid-responsive moderate to severe pain.

4.2 Dose and method of administration

The dose should be adjusted to the intensity of the pain and the sensitivity of the individual patient. The patient's previous history of analgesic requirements, their body weight, and sex (higher plasma concentrations are produced in females), should also be taken into account when determining the dose.

Generally, the lowest effective dose for analgesia should be selected. If higher doses are necessary, increases should be made in 25% - 50% increments where possible.

It is recommended that patients take the medication in a consistent manner in relation to the timing of meals.

Treatment goals and discontinuation.

Before initiating treatment with Oxycodone Hydrochloride Tablets, USP (Immediate Release), (Amneal), a treatment strategy including treatment duration and treatment goals, and a plan for end of the treatment, should be agreed together with the patient, in accordance with pain management guidelines. During treatment, there should be frequent contact between the physician and the patient to evaluate the need for continued treatment, consider discontinuation and to adjust dosages if needed. When a patient no longer requires therapy with oxycodone, it may be advisable to taper the dose gradually to prevent symptoms of withdrawal. In absence of adequate pain control, the possibility of hyperalgesia, tolerance and progression of underlying disease should be considered (see section 4.4).

The correct dosage per individual patient is that which controls the pain with no or tolerable side effects.

Adults, elderly and children over 18 Years

Prior to initiation and titration of doses, refer to the section 4.4 for information on special risk groups such as females and the elderly.

Oxycodone Hydrochloride Tablets, USP (Immediate Release), (Amneal) should be taken at 4-6 hourly intervals. The dosage is dependent on the severity of the pain, and the patient’s previous history of analgesic requirements.

Increasing severity of pain will require an increased dosage of Oxycodone Hydrochloride Tablets, USP (Immediate Release), (Amneal). The correct dosage for any individual patient is that which controls the pain and is well tolerated throughout the dosing period. Patients should be titrated to pain relief unless unmanageable adverse reactions prevent this.

Oxycodone Hydrochloride Tablets, USP (Immediate Release), (Amneal) will generally be used in a short term trial (4-6 weeks) to determine if the pain is opioid responsive, before transferring to a longer acting controlled release oxycodone preparation, in accordance with the clinical guidelines on the use of opioid analgesics in such patients (e.g. those published by the Australian Pain Society in the Medical Journal of Australia 1997; 167: 30-4).

The usual starting dose for opioid-naïve patients or patients presenting with severe pain uncontrolled by weaker opioids is 5mg, 4-6 hourly. The dose should then be carefully titrated, as frequently as once a day if necessary, to achieve pain relief. The majority of patients will not require a daily dose greater than 400 mg. However, a few patients may require higher doses.

Patients receiving oral morphine before oxycodone therapy should have their daily dose based on the following ratio: 10 mg of oral oxycodone is equivalent to 20 mg of oral morphine. It must be emphasized that this is a guide to the dose of Oxycodone Hydrochloride Tablets, USP (Immediate Release), (Amneal) required only. Inter-patient variability requires that each patient be carefully titrated to the appropriate dose.

Controlled pharmacokinetic studies in elderly patients (aged over 65 years) have shown that compared with younger adults, the clearance of oxycodone is only slightly reduced. No untoward adverse reactions were seen based on age, therefore, adult doses and dosage intervals are appropriate.

Transferring patients between oral and parenteral oxycodone:

The dose should be based on the following ratio: 2 mg of oral oxycodone is equivalent to 1 mg of parenteral oxycodone. It must be emphasised that this is a guide to the dose required. Inter-patient variability requires that each patient is carefully titrated to the appropriate dose.

Conversion from morphine:

It must be emphasised that this is a guide to the dose of oxycodone required. Inter-patient variability requires that each patient is carefully titrated to the appropriate dose. Initially, a lower-than-equivalent dose may be advisable.

Patients receiving oral morphine before oxycodone therapy should have their daily dose based on the following ratio: 10 mg of oral oxycodone is equivalent to 20 mg of oral morphine.

Adults with mild to moderate renal impairment and mild hepatic impairment

The plasma concentration in this patient population may be increased. Therefore, dose initiation should follow a conservative approach (refer section 4.4).

The recommended adult starting dose should be reduced by 50%, and each patient should be titrated to adequate pain control according to their clinical situation.

Children under 18 years

Oxycodone Hydrochloride Tablets, USP (Immediate Release), (Amneal)should not be used in patients under 18 years.

Method of administration

Alcoholic beverages should be avoided while the patient is being treated with Oxycodone Hydrochloride Tablets, USP (Immediate Release), (Amneal).

Use in non-malignant pain

Opioids are not first-line therapy for chronic non-malignant pain, nor are they recommended as the only treatment. The need for continued treatment in non-malignant pain should be assessed at regular intervals.

4.3 Contraindications

Hypersensitivity to oxycodone, or to any of the excipients listed in section 6.1, acute respiratory depression, *cor pulmonale*, cardiac arrhythmias, acute asthma or other obstructive airways disease, paralytic ileus, suspected surgical abdomen, severe renal impairment (refer to section 4.4), severe hepatic impairment, delayed gastric emptying, acute alcoholism, brain tumour, increased cerebrospinal or intracranial pressure, head injury (due to risk of raised intracranial pressure), severe CNS depression, convulsive disorders, *delirium tremens*, hypercarbia, concurrent administration of monoamine oxidase inhibitors or within two weeks of discontinuation of their use. Pregnancy (see section 4.6).

Not recommended for pre-operative use.

4.4 Special warnings and precautions for use

Oxycodone has to be administered with caution in the debilitated elderly or patients with:

- Severely impaired respiratory function
- Sleep apnoea
- CNS depressants co-administration (see below and section 4.5)
- Psychological dependence (addiction), abuse profile and history of substance and/or alcohol abuse (see below)
- Intracranial lesions, reduced level of consciousness of uncertain origin
- Hypotension
- Pancreatitis
- Myxedema
- Hypothyroidism
- Addison's disease
- Prostate hypertrophy
- Alcoholism
- Toxic psychosis
- Constipation
- Hypovolaemia
- Inflammatory bowel disorders
- Chronic pulmonary

Hazardous and harmful use

Oxycodone Hydrochloride Tablets, USP (Immediate Release), (Amneal) contain the opioid oxycodone hydrochloride and is a potential medicine of abuse, misuse and addiction. Addiction can occur in patients appropriately prescribed Oxycodone Hydrochloride Tablets, USP (Immediate Release), (Amneal) at recommended doses.

The risk of addiction is increased in patients with a personal or family history of substance abuse (including alcohol and prescription and illicit drugs) or mental illness. The risk also increases the longer the medicine is used and with higher doses. Patients should be assessed for their risks for opioid abuse or addiction prior to being prescribed Oxycodone Hydrochloride Tablets, USP (Immediate Release), (Amneal).

All patients receiving opioids should be routinely monitored for signs of misuse and abuse. Opioids are sought by people with addiction and may be subject to diversion. Strategies to reduce these risks include

prescribing the medicine in the smallest appropriate quantity and advising the patient on the safe storage and proper disposal of any unused medicine (see section 6.4 and section 6.6). Caution patients that abuse of oral forms of opioids by parenteral administration can result in serious adverse events, which may be fatal.

Patients should be advised not to share Oxycodone Hydrochloride Tablets, USP (Immediate Release), (Amneal) with anyone else.

Respiratory depression and sedation

Serious, life-threatening or fatal respiratory depression can occur with the use of opioids even when used as recommended. It can occur at any time during the use of Oxycodone Hydrochloride Tablets, USP (Immediate Release), (Amneal) but the risk is greatest during initiation of therapy or following an increase in dose. Patients should be monitored closely for respiratory depression at these times.

The risk of life-threatening respiratory depression is also higher in elderly, frail, or debilitated patients and in patients with existing impairment of respiratory function (e.g. chronic obstructive pulmonary disease; asthma). Opioids should be used with caution and with close monitoring in these patients (see section 4.2). The use of opioids is contraindicated in patients with severe respiratory disease, acute respiratory disease and respiratory depression (see section 4.3).

The risk of respiratory depression is greater with the use of high doses of opioids, especially high potency and modified release formulations, and in opioid naïve patients. Initiation of opioid treatment should be at the lower end of the dosage recommendations with careful titration of doses to achieve effective pain relief. Careful calculation of equianalgesic doses is required when changing opioids or switching from immediate release to modified release formulations, (see section 4.2).

Opioids can cause sleep-related breathing disorders including central sleep apnoea (CSA) and sleep-related hypoxemia. Opioid use increases the risk of CSA in a dose-dependent fashion. Opioids may also cause worsening of pre-existing sleep apnoea (see section 4.8). In patients who present with CSA, consider decreasing the opioid dosage using best practices for opioid taper.

Risks from concomitant use of benzodiazepines or other CNS depressants, including alcohol

Concomitant use of Oxycodone Hydrochloride Tablets, USP (Immediate Release), (Amneal) and benzodiazepines or other CNS depressants, including alcohol may result in sedation, respiratory depression, coma and death. Because of these risks, concomitant prescribing of Oxycodone Hydrochloride Tablets, USP (Immediate Release), (Amneal) with CNS depressant medicines, such as other opioid analgesics, benzodiazepines, gabapentinoids, cannabis, sedatives, hypnotics, tricyclic antidepressants, antipsychotics, antihistamines, centrally-active anti-emetics and other CNS depressants should be reserved for patients for whom alternative treatment options are not possible. If a decision is made to prescribe Oxycodone Hydrochloride Tablets, USP (Immediate Release), (Amneal) concomitantly with any of the medicines, the lowest effective dose should be used, and the duration of treatment should be as short as possible.

The patients should be followed closely for signs and symptoms of respiratory depression and sedation.

Patients and their caregivers should be made aware of these symptoms. Patients and their caregivers should also be informed of the potential harms of consuming alcohol while taking Oxycodone Hydrochloride Tablets, USP (Immediate Release), (Amneal).

Advise both patients and caregivers about the risks of respiratory depression and sedation when Oxycodone Hydrochloride Tablets, USP (Immediate Release), (Amneal) is used with benzodiazepines or other CNS depressants (including alcohol and illicit drugs). Advise patients not to drive or operate heavy machinery until the effects of concomitant use of the benzodiazepine or other CNS depressant have been determined. Screen patients for risk of substance use disorders, including opioid abuse and misuse, and warn them of the risk for overdose and death associated with the use of additional CNS depressants including alcohol and illicit drugs (see section 4.5).

Use of opioids in chronic (long-term) non-cancer pain (CNCP)

Opioid analgesics have an established role in the treatment of acute pain, cancer pain and palliative and end-of-life care. Current evidence does not generally support opioid analgesics in improving pain and function for most patients with chronic non-cancer pain. The development of tolerance and physical dependence and risks of adverse effects, including hazardous and harmful use, increase with the length of time a patient takes an opioid. The use of opioids for long-term treatment of CNCP is not recommended.

The use of an opioid to treat CNCP should only be considered after maximised non-pharmacological and non-opioid treatments have been tried and found ineffective, not tolerated or otherwise inadequate to provide sufficient management of pain. Opioids should only be prescribed as a component of comprehensive multidisciplinary and multimodal pain management.

Opioid therapy for CNCP should be initiated as a trial in accordance with clinical guidelines and after a comprehensive biopsychosocial assessment has established a cause for the pain and the appropriateness of opioid therapy for the patient (see *Hazardous and harmful use* above). The expected outcome of therapy (pain reduction rather than complete abolition of pain, improved function and quality of life) should be discussed with the patient before commencing opioid treatment, with agreement to discontinue treatment if these objectives are not met.

Owing to the varied response to opioids between individuals, it is recommended that all patients be started at the lowest appropriate dose and titrated to achieve an adequate level of analgesia and functional improvement with minimum adverse reactions. Immediate-release products should not be used to treat chronic pain, but may be used for a short period in opioid-naïve patients to develop a level of tolerance before switching to a modified-release formulation. Careful and regular assessment and monitoring is required to establish the clinical need for ongoing treatment. Discontinue opioid therapy if there is no improvement of pain and/or function during the trial period or if there is any evidence of misuse or abuse. Treatment should only continue if the trial has demonstrated that the pain is opioid responsive and there has been functional improvement. The patient's condition should be reviewed regularly and the dose tapered off slowly if opioid treatment is no longer appropriate (see *Ceasing opioids* below).

Tolerance, dependence and withdrawal

Neuroadaptation of the opioid receptors to repeated administration of opioids can produce tolerance and physical and/or psychological dependence.

Abuse and addiction are separate and distinct from physical dependence and tolerance. Healthcare providers should be aware that addiction may not be accompanied by concurrent tolerance and symptoms of physical dependence in all addicts. In addition, abuse of opioids can occur in the absence of true addiction.

Tolerance is the need for increasing doses to maintain analgesia. Tolerance may occur to both the desired and undesired effects of the opioid and may develop at different rates for different effects. In the case of opioids, such as oxycodone, tolerance usually develops more slowly to analgesia than to respiratory depression, and tolerance to the constipating effects may not occur at all. Tolerance to the analgesic effects of opioids is variable in occurrence but not absolute.

The patient may develop analgesic tolerance to the medicine with chronic use and may require progressively higher doses to maintain pain control (in the absence of disease progression or other external factors). Physical dependence, which can occur after several days to weeks of continued opioid usage, results in withdrawal symptoms if the opioid is ceased abruptly or the dose is significantly reduced.

Withdrawal symptoms can also occur following the administration of an opioid antagonist (e.g. naloxone) or partial agonist (e.g. buprenorphine). Withdrawal can result in some or all of the following symptoms: dysphoria, restlessness/agitation, lacrimation, rhinorrhoea, yawning, sweating, chills, myalgia, mydriasis, irritability, anxiety, increasing pain, backache, joint pain, weakness, abdominal cramps, insomnia, nausea, anorexia, vomiting, diarrhoea, increased blood pressure, increased respiratory rate and increased heart rate.

When discontinuing Oxycodone Hydrochloride Tablets, USP (Immediate Release), (Amneal) in a person who may be physically-dependent, the medicine should not be ceased abruptly but withdrawn by tapering the dose gradually (see *Ceasing opioids* below and section 4.2). Given the increased risk for serious harms associated with increasing doses, opioid use should be limited to the minimum needed to manage pain which can help limit development of tolerance and therefore of withdrawal once opioids are discontinued.

Opioid Use Disorder* (abuse and dependence)

Repeated use of Oxycodone Hydrochloride Tablets, USP (Immediate Release), (Amneal) may lead to Opioid Use Disorder (OUD). A higher dose and longer duration of opioid treatment may increase the risk of developing OUD. Abuse or intentional misuse of Oxycodone Hydrochloride Tablets, USP (Immediate Release), (Amneal) may result in overdose and/or death. The risk of developing OUD is increased in patients with a personal or a family history (parents or siblings) of substance use disorders (including alcohol use disorder), in current tobacco users or in patients with a personal history of other mental health disorders (e.g. major depression, anxiety and personality disorders).

Before initiating treatment with Oxycodone Hydrochloride Tablets, USP (Immediate Release), (Amneal) and during the treatment, treatment goals and a discontinuation plan should be agreed with the patient (see section 4.2). Before and during treatment the patient should also be informed about the risks and signs of OUD. If these signs occur, patients should be advised to contact their physician.

Patients will require monitoring for signs of drug-seeking behaviour (e.g. too early requests for refills). The prescriber should conduct a review of concomitant opioids and psycho-active medicines (like benzodiazepines). For patients with signs and symptoms of OUD, consultation with an addiction specialist should be considered.

* Opioid Use Disorder is a problematic pattern of opioid use leading to clinically significant impairment or distress. OUD has also been classified as Opioid Abuse or Opioid Dependence and has been referred to as "opioid addiction". Diagnostic criteria for OUD include Tolerance and withdrawal, yet these criteria are not considered to be met for individuals taking opioids solely under appropriate medical supervision.

Accidental ingestion/exposure

Accidental ingestion or exposure of Oxycodone Hydrochloride Tablets, USP (Immediate Release), (Amneal) especially by children, can result in a fatal overdose of oxycodone. Patients and their caregivers should be given information on safe storage and disposal of unused Oxycodone Hydrochloride Tablets, USP (Immediate Release), (Amneal) (see section 6.4 and section 6.6).

Hyperalgesia

Hyperalgesia may occur with the use of opioids, particularly at high doses. Hyperalgesia may manifest as an unexplained increase in pain, increased levels of pain with increasing opioid dosages or diffuse sensitivity not associated with the original pain. Hyperalgesia should not be confused with tolerance (see *Tolerance, dependence and withdrawal* above). If opioid induced hyperalgesia is suspected, the dose should be reduced and tapered off if possible. A change to a different opioid may be required.

Ceasing opioids

Abrupt discontinuation or rapid decreasing of the dose in a person physically dependent on an opioid may result in serious withdrawal symptoms and uncontrolled pain (see *Tolerance, dependence and withdrawal* above). Such symptoms may lead the patient to seek other sources of licit or illicit opioids. Opioids should not be ceased abruptly in a patient who is physically dependent but withdrawn by tapering the dose slowly. Factors to take into account when deciding how to discontinue or decrease therapy include the dose and duration of the opioid the patient has been taking, the type of pain being treated and the physical and psychological attributes of the patient. A multimodal approach to pain management should be in place before initiating an opioid analgesic taper. During tapering, patients require regular review and support to manage any increase in pain, psychological distress and withdrawal symptoms.

There are no standard tapering schedules suitable for all patients and an individualised plan is necessary. In general, tapering should involve a dose reduction of no more than 10% to 25% every 2 to 4 weeks (see section 4.2). If the patient is experiencing increased pain or serious withdrawal symptoms, it may be necessary to go back to the previous dose until stable before proceeding with a more gradual taper.

When ceasing opioids in a patient who has a suspected opioid use disorder, the need for medication assisted treatment and/or referral to a specialist should be considered.

Pre- and post-operative use

As with all opioid preparations, patients who are to undergo cordotomy or other pain-relieving surgical procedures should not receive Oxycodone Hydrochloride Tablets, USP (Immediate Release), (Amneal) for 6 hours before surgery. As with all opioid preparations, Oxycodone Hydrochloride Tablets, USP (Immediate Release), (Amneal) should be used with caution pre-operatively and within the first 12-24 hours post-operatively. Caution should be used in abdominal surgery as opioids are known to impair intestinal motility and should not be used until the physician is assured of normal bowel function. Should paralytic ileus be suspected or occur during use, Oxycodone Hydrochloride Tablets, USP (Immediate Release), (Amneal) should be discontinued immediately.

Effects on hypothalamic-pituitary-adrenal or gonadal axes

Opioids, such as oxycodone hydrochloride, may influence the hypothalamic-pituitary-adrenal or gonadal axes. Some changes that can be seen include an increase in serum prolactin, and decreases in plasma cortisol and testosterone. Clinical symptoms may manifest from these hormonal changes. As with all opioids, a reduction in dosage may be advisable in hypothyroidism.

Hepatobiliary disorders

Oxycodone may cause dysfunction and spasm of the Sphincter of Oddi, thus increasing the risk of biliary tract symptoms and pancreatitis. Therefore, oxycodone has to be administered with caution in patients with pancreatitis and diseases of the biliary tract.

Special Risk Groups

Use in renal and hepatic impairment

In renal and hepatic impairment, the administration of oxycodone does not result in significant levels of active metabolites. However, the plasma concentration of oxycodone in this patient population may be increased compared with patients having normal renal or hepatic function. Therefore, initiation of dosing in patients with renal impairment (CLcr<60mL/min) or hepatic impairment should be reduced to ½ of the usual dose with cautious titration.

Use in the elderly

The plasma concentrations of oxycodone are only nominally affected by age, being approximately 15% greater in elderly as compared with young subjects. There were no differences in adverse event reporting between young and elderly subjects.

Use in the elderly, debilitated patients

As with other opioid initiation and titration, doses in elderly patients who are debilitated should be reduced to ⅓ to ½ of the usual doses.

Gender

Female subjects have, on average, plasma oxycodone concentrations up to 25% higher than males on a body weight adjusted basis. The reason for this difference is unknown. There were no significant male/female differences detected for efficacy or adverse events in clinical trials.

4.5 Interaction with other medicines and other forms of interaction

Anticholinergic agents

Concomitant administration of oxycodone with anticholinergics or medications with anticholinergic activity (e.g. tricyclic antidepressants, antihistamines, antipsychotics, muscle relaxants, anti-Parkinson medications) may result in increased anticholinergic adverse effects.

Antihypertensive agents

Hypotensive effects of these medications may be potentiated when used concurrently with oxycodone, leading to increased risk of orthostatic hypotension.

CNS Depressants

The concomitant use of opioids with sedative medicines such as benzodiazepines or related medicines, increases the risk of sedation, respiratory depression, coma and death because of additive CNS depressant effect.

Reserve concomitant prescribing of these medicines for use in patients for whom alternative treatment options are inadequate. The dose and duration of concomitant use should be limited. Follow patients closely for signs of respiratory depression and sedation (see section 4.4).

Medicines which depress the CNS include, but are not limited to: other opioids, gabapentinoids such as pregabalin, anxiolytics, hypnotics and sedatives (incl. benzodiazepines), tranquilizers, muscle relaxants, medicines with antihistamine-sedating actions such as antipsychotics, antidepressants, phenothiazines and alcohol.

Intake of alcoholic beverages while being treated with Oxycodone Hydrochloride Tablets, USP (Immediate Release), (Amneal) should be avoided because this may lead to more frequent undesirable effects such as somnolence and respiratory depression. Oxycodone hydrochloride containing products should be avoided in patients with a history of or present alcohol, drug or medicines abuse.

Coumarin derivatives

Although there is little substantiating evidence, opiate agonists have been reported to potentiate the anticoagulant activity of coumarin derivatives.

CYP2D6 and CYP3A4 inhibitors and inducers

Oxycodone is metabolized mainly by CYP3A4 with a contribution from CYP2D6. The activities of these metabolic pathways may be inhibited or induced by various co-administered medicines or dietary elements. Oxycodone doses may need to be adjusted accordingly.

CYP3A4 inhibitors, such as macrolide antibiotics (e.g. clarithromycin), azole-antifungal agents (e.g. ketoconazole), protease inhibitors (e.g. ritonavir), and grapefruit juice may cause decreased clearance of oxycodone which could lead to an increase in oxycodone plasma concentrations. Oxycodone metabolism may be blocked by a variety of medicines (e.g. cimetidine, certain cardiovascular medications and antidepressants), although such blockade has not yet been shown to be of clinical significance with Oxycodone Hydrochloride Tablets, USP (Immediate Release), (Amneal).

CYP3A4 inducers, such as rifampin, carbamazepine, phenytoin and St John's wort, may induce the metabolism of oxycodone and cause increased clearance of the medicine, resulting in a decrease in oxycodone plasma concentrations.

Medicines that inhibit CYP2D6 activity, such as paroxetine and quinidine, may cause decreased clearance of oxycodone which could lead to an increase in oxycodone plasma concentrations. Concurrent administration of quinidine does not alter the pharmacodynamic effects of oxycodone.

Oxycodone did not inhibit the activity of P450 isozymes 2D6, 3A4, 1A2, 2A6, 2C19 or 2E1 in human liver microsomes *in vitro*. Non-clinical data *in vitro* and *in vivo* indicate that oxycodone can act as a P-glycoprotein substrate and can induce overexpression of P-glycoprotein in rats.

Metoclopramide

Concurrent use with oxycodone may antagonise the effects of metoclopramide on gastrointestinal motility.

Monoamine Oxidase Inhibitors (MAOIs)

Non-selective MAOIs intensify the effects of opioid agents which can cause anxiety, confusion and significant respiratory depression. Severe and sometimes fatal reactions have occurred in patients concurrently administered MAOIs and pethidine. Oxycodone should not be given to patients taking non-selective MAOIs or within 14 days of stopping such treatment. As it is unknown whether there is an interaction between selective MAOIs (e.g. selegiline) and oxycodone, caution is advised with this medicine combination.

Neuromuscular blocking agents

Oxycodone may enhance the effects of neuromuscular blocking agents resulting in increased respiratory depression.

Opioid agonist analgesics (including morphine, pethidine)

Additive CNS depressant, respiratory depressant and hypotensive effects may occur if two or more opioid agonist analgesics are used concurrently.

Opioid agonist-antagonist analgesics (including pentazocine, butorphanol, buprenorphine)

Mixed agonist/antagonist analgesics may reduce the analgesic effect of oxycodone and/or may precipitate withdrawal symptoms.

Selective Serotonin Re-uptake Inhibitor (SSRI) or a Serotonin Norepinephrine Re-uptake Inhibitor (SNRI)

Concurrent administration of oxycodone with serotonin agents, such as a Selective Serotonin Re-uptake Inhibitor (SSRI) or a Serotonin Norepinephrine Re-uptake Inhibitor (SNRI) may cause serotonin toxicity. The symptoms of serotonin toxicity may include mental-status changes (e.g., agitation, hallucinations, coma), autonomic instability (e.g., tachycardia, labile blood pressure, hyperthermia), neuromuscular abnormalities (e.g., hyperreflexia, incoordination, rigidity), and/or gastrointestinal symptoms (e.g., nausea, vomiting, diarrhoea). Oxycodone Hydrochloride Tablets, USP (Immediate Release), (Amneal) should be used with caution and the dosage may need to be reduced in patients using these medications.

4.6 Fertility, pregnancy and lactation

Pregnancy

Australian Pregnancy Category C: Medicines which, owing to their pharmacological effects, have caused or may be suspected of causing, harmful effects on the human fetus or neonate without causing malformations. These effects may be reversible.

Oxycodone used during pregnancy or labour, may cause withdrawal symptoms and/or respiratory depression in the newborn infant. Oral administration of oxycodone during the period of organogenesis did not elicit teratogenicity or embryofoetal toxicity in rats or rabbits at doses up to 8 mg/kg/day in rats (equivalent to 17 mg/day in women, based on estimated plasma AUC values) or 125 mg/kg/day in rabbits.

Oral administration of oxycodone to rats from early gestation to weaning did not affect post-natal development parameters at doses up to 6 mg/kg/day (equivalent to 9 mg/day in women, based on estimated AUC values). In a study designed specifically to investigate the effect of pre-natal oxycodone on the hypothalamic-pituitary-adrenal axis in adolescent rats, intravenous administration of oxycodone 0.8 mg/kg/day (equivalent to 11 mg/day in pregnant women, based on estimated AUC values) had no effect on the corticosterone response, but delayed and enhanced the peak ACTH response to corticotrophin releasing hormone in males, but not females. The clinical significance of this observation is unknown.

There are no adequate and well controlled studies with oxycodone in pregnant women. Because animal reproduction studies are not always predictive of human responses, oxycodone should not be used during pregnancy unless clearly needed. Prolonged use of oxycodone during pregnancy can result in neonatal opioid withdrawal syndrome. Oxycodone is not recommended for use in women during or immediately prior to labour. Infants born to mothers who have received opioids during pregnancy should be monitored for respiratory depression.

The medicine penetrates the placenta. Therefore, the use of this medicinal product should be avoided to the extent possible in patients who are pregnant.

Breastfeeding

Use of this medicinal product should be avoided to the extent possible in patients who are lactating. Oxycodone accumulates in human milk, with a median maternal milk:plasma ratio of 3:1 recorded in one study. Oxycodone (7.5 ng/mL) was detected in the plasma of one of forty-one infants 72 hours after Caesarean section. Opioids may cause respiratory depression in the newborn and withdrawal symptoms can occur in breastfeeding infants when maternal administration of an opioid analgesic is stopped. Oxycodone Hydrochloride Tablets, USP (Immediate Release), (Amneal) should not be used in breastfeeding mothers unless the benefits outweigh the risks. Breastfed infants should be monitored for respiratory depression, sedation, poor attachment and gastrointestinal signs.

Fertility

No human data on the effect of oxycodone on fertility are available. In rats, there was no effect on mating or fertility with oxycodone treatment (see section 5.3).

Despite these fertility studies in animals, prolonged use of opioids may result in impairment of reproductive function, including fertility and sexual dysfunction in both sexes, and irregular menses in women.

4.7 Effects on ability to drive and use machines

Oxycodone may modify patients' reactions to a varying extent depending on the dosage and individual susceptibility. If affected, patients should not drive or operate machinery.

4.8 Undesirable effects

Oxycodone Hydrochloride Tablets, USP (Immediate Release), (Amneal) may have a higher incidence of some adverse reactions than oxycodone controlled-release formulations. Anticipation of adverse reactions and appropriate patient management can improve acceptability.

Tabulated summary of adverse reactions

	Very Common (≥1/10)	**Common (1/100 to <1/10)**	**Uncommon (1/1,000 to <1/100)**	**Rare (≥1/10,000 to <1/1,000)**	**Not known (cannot be estimated from the available data)**
Immune system disorders			Hypersensitivity		Anaphylactic reaction, Anaphylactoid reaction
Metabolic and nutritional disorders		Decreased appetite	Dehydration		
Psychiatric disorders		Anxiety, Confusional state, Insomnia, Nervousness, Thinking abnormal, Depression	Affect lability, Agitation, Dysphoria, Euphoric mood, Hallucination, Libido decreased		Aggression, Drug dependence*
Nervous system disorders	Dizziness, Headache, Somnolence	Tremor, Lethargy	Amnesia, Convulsion, Hypertonia, Hypoaesthesia, Muscle contractions involuntary, Paraesthesia, Speech disorder, Syncope, Dysgeusia (taste perversion)		Hyperalgesia
Eye disorders			Miosis, Visual impairment		
Ear and labyrinth disorders			Vertigo		
Cardiac disorders			Palpitations (as part of withdrawal syndrome)		
Vascular disorders			Vasodilation	Hypotension, Orthostatic hypotension	

	Very Common (≥1/10)	Common (1/100 to <1/10)	Uncommon (1/1,000 to <1/100)	Rare (≥1/10,000 to <1/1,000)	Not known (cannot be estimated from the available data)
Respiratory, thoracic and mediastinal disorders		Dyspnoea	Respiratory depression		Central sleep apnoea syndrome
Gastrointestinal disorders	Constipation, Nausea, Vomiting	Abdominal pain, Diarrhoea, Dry mouth, Dyspepsia	Dysphagia, Eructation, Flatulence, Illeus		Dental caries
Hepatobiliary disorders			Hepatic enzymes increased		Cholestasis
Skin and subcutaneous tissue disorders	Pruritis	Hyperhidrosis, Rash	Dry skin	Urticaria	
Renal and urinary disorders			Urinary retention		
Reproductive system and breast disorders			Erectile dysfunction, Hypogonadism		Amenorrhoea
General disorders and administration site conditions		Asthenia, Fatigue	Chills, Oedema, Peripheral oedema, Malaise, Thirst		Drug withdrawal syndrome neonatal, Opioid tolerance**, Opioid withdrawal syndrome**

* The frequency of drug dependence cannot be estimated from available evidence (e.g. clinical trials, spontaneous reporting, and the medical literature) and therefore is classified as "not known" (see *Drug Dependence* below). 'Not known' should not be interpreted as an indication of the rarity of the occurrence of drug dependence, but a reflection of the limitations in the available evidence that do not support a precise estimate of frequency.

** The frequency of opioid tolerance and the frequency of opioid withdrawal syndrome cannot be estimated from available evidence (e.g. clinical trials, spontaneous reporting, and the medical literature) and therefore is classified as "not known" (see *Opioid Tolerance and Opioid Withdrawal Syndrome* below). 'Not known' should not be interpreted as an indication of the rarity of the occurrence of opioid tolerance and opioid withdrawal syndrome, but a reflection of the limitations in the available evidence that do not support a precise estimate of frequency.

If nausea and vomiting are troublesome, oxycodone may be combined with an antiemetic. Constipation must be treated with appropriate laxatives. Overdose may produce respiratory depression. Compared with other opioids, oxycodone is associated with low histamine release although urticaria and pruritus may occur.

Drug Dependence

The frequency in the above table regarding drug dependence reflects the current evidence, including cumulative data from clinical trials and additional post marketing sources, and indicates that the risk of drug dependence with opioids is highly variable depending upon: definition of drug dependence; duration of treatment; dose; individual patient risk factors; and clinical settings. 'Not known' should not be interpreted as an indication of the rarity of the occurrence of drug dependence, but a reflection of the limitations in the available evidence that do not support a precise estimate of frequency.

Repeated use of Oxycodone Hydrochloride Tablets, USP (Immediate Release), (Amneal) may lead to drug dependence, even at therapeutic doses. The risk of drug dependence may vary depending on a patient's individual risk factors, dosage, and duration of opioid treatment (see section 4.4 for monitoring and risk reduction interventions).

As an opioid, oxycodone exposes users to the risks of dependence (both physical and psychological), addiction, abuse, and misuse, as well as opioid use disorder and problematic opioid use. Although the risk of addiction in any individual is unknown, it can occur in patients appropriately prescribed oxycodone. Addiction can occur at recommended doses, and if the medicine is misused or abused. Risks are increased in patients with a personal or family history of substance abuse (including drug or alcohol abuse or addiction) or mental illness (e.g. major depression). The frequency of drug dependence also increases with longer term use or higher doses of oxycodone.

See section 4.4 on monitoring and risk reduction interventions.

Opioid Tolerance and Opioid Withdrawal Syndrome

The frequency in the above table regarding opioid tolerance and opioid withdrawal syndrome reflects the high variability of risk depending upon: definition of tolerance and withdrawal syndrome; dose and duration of treatment; and assessment and monitoring methods (specific to withdrawal syndrome). 'Not known' should not be interpreted as an indication of the rarity of the occurrence of opioid tolerance and opioid withdrawal syndrome, but a reflection of the limitations in the available evidence that do not support a precise estimate of frequency. As an opioid, oxycodone exposes users to the risks of dependence (both physical and psychological), tolerance and withdrawal syndrome.

See section 4.4 on monitoring and risk reduction interventions.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://pophealth.my.site.com/carmreportnz/s/.

4.9 Overdose

Acute overdosage with oxycodone can be manifested by respiratory depression (reduced respiratory rate and/or tidal volume, Cheyne-Stokes respiration, cyanosis), extreme somnolence progressing to stupor or coma, hypotonia, skeletal muscle flaccidity, cold and/or clammy skin, miosis (dilated if hypoxia is severe), and sometimes bradycardia, hypoglycaemia, hypotension, and death. Severe overdose may result in apnoea, pulmonary oedema, circulatory collapse and death.

Toxic leukoencephalopathy has been observed with oxycodone overdose.

Primary attention should be given to immediate supportive therapy with the establishment of adequate respiratory exchange through the provision of a patent airway and institution of assisted or controlled ventilation. Adequate body temperature and fluid balance should be maintained.

Oxygen, intravenous fluids, vasopressors and other supportive measures should be used as indicated to manage the circulatory shock accompanying an overdose. The opioid antagonist naloxone hydrochloride is a specific antidote for respiratory depression due to overdosage or as a result of unusual sensitivity.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

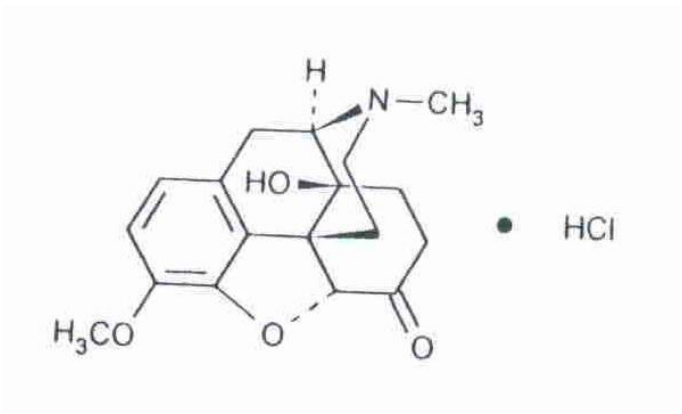
5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Natural opium alkaloids
ATC code: N02AA05

Non-proprietary name: Oxycodone hydrochloride
Chemical name: 4,5α-epoxy-14-hydroxy-3-methoxy-17-methylmorphinan-6-one hydrochloride
CAS No.: 124-90-3
Molecular formula: $C_{18}H_{21}NO_4HCl$
Molecular weight: 351.83

The structural formula for oxycodone hydrochloride is:



Oxycodone hydrochloride is a white, crystalline, odourless powder readily soluble in water, sparingly soluble in ethanol and nearly insoluble in ether.

Mechanism of Action

Oxycodone is a full opioid agonist with no antagonist properties whose principal therapeutic action is analgesia. It has affinity for kappa, mu and delta opiate receptors in the brain and spinal cord. Oxycodone is similar to morphine in its action.

Pharmacodynamic effects

Other pharmacological actions of oxycodone are in the central nervous system (CNS: respiratory depression, antitussive, anxiolytic, sedative and miosis), smooth muscle (constipation, reduction in gastric, biliary and pancreatic secretions, spasm of sphincter of Oddi and transient elevations in serum amylase) and cardiovascular system (release of histamine and/or peripheral vasodilatation, possibly causing pruritus, flushing, red eyes, sweating and/or orthostatic hypotension).

Opioids, such as oxycodone hydrochloride, may influence the hypothalamic-pituitary-adrenal or gonadal axes. Some changes that can be seen include an increase in serum prolactin, and decreases in plasma cortisol and testosterone. Clinical symptoms may manifest from these hormonal changes.

In vitro and animal studies indicate various effects of natural opioids, such as morphine, on components of the immune system; the clinical significance of these findings is unknown. Whether oxycodone, a semisynthetic opioid, has immunological effects similar to morphine is unknown.

This medicine has been given a provisional consent under Section 23 of the Act to address an urgent shortage in the market with the following condition: the medicine may only be marketed or distributed when no other oxycodone hydrochloride immediate-release oral dosage form medicine with consent under section 20 of the Medicines Act 1981 is available in the New Zealand market, or to meet sole tender obligations.

5.2 Pharmacokinetic properties

Absorption

Compared with morphine, which has an absolute bioavailability of approximately 30%, oxycodone undergoes relatively low “first-pass” metabolism and has a high absolute bioavailability of up to 87% following oral administration. Maximum oxycodone plasma concentrations are achieved after approximately 1 to 1.5 hours after the intake.

No data are available on the effect of food on the absorption of Oxycodone Hydrochloride Tablets, USP (Immediate Release), (Amneal).

Distribution

Following absorption, oxycodone is distributed throughout the entire body. Approximately 45% is bound to plasma protein.

Biotransformation and Elimination

Apparent elimination half-life of oxycodone following the administration of oxycodone hydrochloride was 3.5 to 4 hours.. The active medicine and its metabolites are excreted in both urine and faeces and is metabolised in the liver to form noroxycodone, oxymorphone, noroxymorphone, 6α and β oxycodol and conjugated glucuronides. CYP3A4 and CYP2D6 are involved in the formation of noroxycodone and oxymorphone, respectively (see section 4.5). The contribution of these metabolites to the analgesic effect is insignificant.

5.3 Preclinical safety data

Reproductive and Developmental Toxicology

Oxycodone had no effect on fertility or early embryonic development in male and female rats at doses as high as 8 mg/kg/day. Also, oxycodone did not induce any malformations in rats at doses as high as 8 mg/kg/day or in rabbits at doses as high as 125 mg/kg/day. Dose-related increases in developmental variations (increased incidences of extra (27) presacral vertebrae and extra pairs of ribs) were observed in rabbits when the data for individual fetuses were analyzed. However, when the same data were analyzed using litters as opposed to individual fetuses, there was no dose-related increase in developmental variations although the incidence of extra presacral vertebrae remained significantly higher in the 125 mg/kg/day group compared to the control group. Since this dose level was associated with severe pharmacotoxic effects in the pregnant animals, the fetal findings may have been a secondary consequence of severe maternal toxicity.

In a prenatal and postnatal development study in rats, maternal body weight and food intake parameters were reduced for doses ≥2 mg/kg/day compared to the control group. Body weights were lower in the F1 generation from maternal rats in the 6 mg/kg/day dosing group. There were no effects on physical, reflexological, or sensory developmental parameters or on behavioral and reproductive indices in the F1 pups (the NOEL for F1 pups was 2 mg/kg/day based on body weight effects seen at 6 mg/kg/day). There were no effects on the F2 generation at any dose in the study.

Carcinogenicity

Carcinogenicity was evaluated in a 2-year oral gavage study conducted in Sprague-Dawley rats. Oxycodone did not increase the incidence of tumors in male and female rats at doses up to 6 mg/kg/day. The doses were limited by opioid-related pharmacological effects of oxycodone

Genotoxicity

The results of *in vitro* and *in vivo* studies indicate that the genotoxic risk of oxycodone to humans is minimal or absent at the systemic oxycodone concentrations that are achieved therapeutically. Oxycodone was not genotoxic in a bacterial mutagenicity assay or in an *in vivo* micronucleus assay in the mouse. Oxycodone produced a positive response in the *in vitro* mouse lymphoma assay in the presence of rat liver S9 metabolic activation at dose levels greater than 25 µg/mL. Two *in vitro* chromosomal aberrations assays with human lymphocytes were conducted. In the first assay, oxycodone was negative without metabolic activation but was positive with S9 metabolic activation at the 24 hour time point but not at 48 hours after exposure. In the second assay, oxycodone did not show any clastogenicity either with or without metabolic activation at any concentration or time point.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Each tablet contains the following inactive ingredients: corn starch, lactose monohydrate, microcrystalline cellulose, sodium starch glycolate and stearic acid.

The 10 mg tablets also contain the colourant D&C Red No. 27.

The 20 mg tablets also contain the colourants FD&C Blue No. 2, FD&C Red No. 40 and FD&C Yellow No. 6.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

2 years

6.4 Special precautions for storage

Store below 25°C, protected from moisture.

Store securely, out of sight and reach of children, and in a location not accessible by others, including visitors to the home.

6.5 Nature and contents of container

Oxycodone Hydrochloride Tablets, USP (Immediate Release), (Amneal) come in HDPE bottles with a child-resistant closure and a rayon coil.

Pack size: 100 tablets

6.6 Special precautions for disposal

Any unused medicine or waste material should be disposed of in accordance with local requirements.

7. MEDICINE SCHEDULE

Controlled Drug B3

8. SPONSOR

Wellmed.NZ Limited
Level 1
50 Customhouse Quay
Wellington 6011

Ph: 0800 488 866

9. DATE OF FIRST APPROVAL

12 July 2024

10. DATE OF REVISION OF THE TEXT

26 June 2025

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
4.4	Removed 'Tolerance, physical dependence and withdrawal' as a bullet point under caution in the deliberated elderly or patients with. Is included as a separate point in this section. Added hepatobiliary disorders.
4.5	Added Selective Serotonin Re-uptake Inhibitors (SSRI) and Serotonin Norepinephrine Re-uptake Inhibitors (SNRI).
4.9	Hypoglycaemia added as a possible overdose symptom.