OxyNorm® *Capsules*

Composition

Oxycodone hydrochloride Ph Eur

Oxycodone hydrochloride is a white, crystalline odourless powder readily soluble in water, sparingly soluble in ethanol and nearly insoluble in ether. The chemical name is 4,5α-epoxy-14-hydroxy-3-methoxy-17-methylmorphinan-6-one hydrochloride (CAS No: 124-90-3). The molecular formula is $C_{18}H_{21}NO_4$ HCl and molecular weight is 351.83.

The inactive ingredients in ***OxyNorm®*** capsules are: microcrystalline cellulose and magnesium stearate.

The capsule shells contain sodium lauryl sulfate and gelatin. Capsule shell is derived from animal origin (bovine source).

The capsule shells also contain the following colouring materials:

	Strength		
Colouring material	**5 mg**	**10 mg**	**20 mg**
Indigo carmine CI73015 (E132)	•	•	•
Iron oxide red CI77491 (E172)	•	•	•
Iron oxide yellow CI77492 (E172)	•	•	•
Sunset yellow FCF CI15985 (E110)	•		
Titanium dioxide (E171)	•	•	•

Therapeutic properties

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. Other pharmacological actions of oxycodone are in the 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 vasodilation, possibly causing pruritus, flushing, red eyes, sweating and/or orthostatic hypotension).

Pharmacokinetics

Elimination and Metabolism

Oxycodone has an elimination half life of approximately 3 hours and is metabolised principally to noroxycodone and oxymorphone. Oxymorphone has some analgesic activity but is present in plasma in low concentrations and is not considered to contribute to oxycodone's pharmacological effect.

Oxycodone hydrochloride is metabolised in the intestines and liver to form noroxycodone, oxymorphone and other conjugated glucuronides. CYP3A4 and CYP2D6 are probably involved in the formation of noroxycodone and oxymorphone, respectively. The contribution of these metabolites to the analgesic effect is insignificant.

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. Peak plasma concentrations of oxycodone are reached approximately 1 hour after administration of ***OxyNorm®*** capsules.

No data are available on the effect of food on the absorption of OxyNorm® capsules. Limited data indicated that absorption of oxycodone from an oral solution may be significantly affected by food. An increase in mean AUC of approximately 20% and decrease in Cmax of approximately 20% have been reported.

Indication
The management of opioid responsive, moderate to severe pain.

Contraindications
Hypersensitivity to opioids and to any of the constituents or in any situation where opioids are contraindicated, severe respiratory depression with hypoxia, cor pulmonale, cardiac arrhythmias, severe bronchial asthma,, chronic bronchial asthma or other chronic obstructive airways disease, elevated carbon dioxide levels in the blood,paralytic ileus, acute abdomen, moderate to severe hepatic impairment, severe renal impairment (creatinine clearance < 10 mL/min), delayed gastric emptying, acute alcoholism, brain tumor, increased cerebrospinal or intracranial pressure, head injury, severe CNS depression, convulsive disorders, delirium tremens, hypercarbia, chronic constipation, concurrent administration of monoamine oxidase inhibitors or within 2 weeks of discontinuation of their use. Not recommended for pre-operative use.

Use in fertility, pregnancy and lactation

<u>Pregnancy</u>
Category C: Oxycodone, when used during labour, may cause respiratory depression in the new born. ***OxyNorm®*** capsules are not recommended for use in pregnancy nor during labour.
There are limited data from the use of oxycodone in pregnant women. Regular use in pregnancy may cause drug dependence in the foetus, leading to withdrawal symptoms in the neonate. If opioid use is required for a prolonged period in pregnant women, advise the patient of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available.

Administration during labour may depress respiration in the neonate and an antidote for the child should be readily available.

<u>Breastfeeding</u>

Administration to nursing women is not recommended as oxycodone may be secreted in breast milk and may cause respiratory depression in the infant.

Drug interactions and incompatibilities

The concomitant use of opioids with sedative medicines such as benzodiazepines or related drugs increases the risk of sedation, respiratory depression, coma and death because of additive CNS depressant effect. The dosage and duration of concomitant use should be limited (see section Warnings & Precautions).

Drugs which affect the CNS include, but are not limited to: other opioids, gabapentinoids such as pregabalin, anxiolytics, hypnotics and sedatives (including benzodiazepines), antipsychotics, antidepressants, phenothiazines, anaesthetics, muscle relaxants, antihypertensives, alcohol, tranquillisers, non-benzodiazepine sedatives and neuroleptic drugs. Concomitant 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 should be used with caution and the dosage may need to be reduced in patients using these medications.

Concomitant administration of oxycodone with anticholinergics or medicines with anticholinergic activity (e.g. tricyclic anti-depressants, antihistamines, antipsychotics, muscle relaxants, anti-Parkinson drugs) may result in increased anticholinergic adverse effects. Oxycodone should be used with caution and the dosage may need to be reduced in patients using these medications.

Anticholinergic agents
Concurrent use with oxycodone may result in an increased anticholinergic adverse effects.and increased risk of severe constipation and/or urinaryretention.

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

CNS depressants (including sedatives or hypnotics, general anaesthetics, phenothiazines, other tranquillisers, alcohol, other opioids and neuroleptic drugs, etc.)
Concurrent use with oxycodone may result in increased respiratory depression, hypotension, profound sedation or coma. Caution is recommended and the dosage of one or both agents should be reduced.

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

Metoclopramide

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

Monoamine Oxidase Inhibitors (MAOIs)

MAO inhibitors are known to interact with narcotic analgesics. MAO-inhibitors cause CNS excitation or depression associated with hypertensive or hypotensive crisis (see Section Warnings and Precautions). Co-administration with monoamine oxidase inhibitors or within two weeks of discontinuation of their use should be avoided. Non-selective MAOIs intensify the effects of opioid drugs which can cause anxiety, confusion, CNS excitation or depression associated with hypertensive or hypotensive crisis. 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 drug combination.

Alcohol may enhance the pharmacodynamic effects of OxyNorm, concomitant use should be avoided.

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.

Oxycodone is metabolised mainly by CYP3A4, with a contribution from CYP2D6. The activities of these metabolic pathways may be inhibited or induced by various co-administered drugs or dietary elements. Oxycodone doses may need to be adjusted accordingly. Metabolic interactions with drugs that involve the cytochrome P450 enzyme system (CYP3A4, CYP2D6) can cause the plasma concentration of oxycodone to increase. Quinidine, which is a potent CYP2D6 inhibitor, has blocked the formation of oxymorphone, while the oxycodone concentration increased marginally. Concurrent administration of quinidine does not alter the pharmacodynamic effects of oxycodone. The metabolic pathway may be blocked by a variety of drugs (e.g. cimetidine, certain cardiovascular drugs and antidepressants), although such blockade has not yet been shown to be of clinical significance with ***OxyNorm®*** capsules. Inhibitors of cytochrome P450-3A such as ketoconazole and erythromycin may inhibit the metabolism of oxycodone.

The potential effects of oxycodone on CYP enzyme have not been studied either *in vitro or in vivo*.

CYP3A4 inhibitors, such as macrolide antibiotics (e.g. clarithromycin, erythromycin and telithromycin), azole-antifungals (e.g. ketoconazole, voriconazole, itraconazole, and posaconazole), protease inhibitors (e.g. boceprevir, ritonavir, indinavir, nelfinavir and saquinavir), cimetidine and grapefruit juice may cause a reduced clearance of oxycodone that could cause an increase of the plasma concentrations of oxycodone. Therefore, the oxycodone dose may need to be adjusted accordingly.

Warnings and precautions

The primary risk of opioid excess is respiratory depression. Caution must be exercised when administering oxycodone to the debilitated elderly; opioid dependent patients, patients with severely impaired pulmonary function, patients with impaired hepatic or renal function, patients with myxedema, hypothyroidism, Addison's disease, toxic psychosis, prostatic hypertrophy, adrenocortical insufficiency, alcoholism, delirium tremens, diseases of the biliary tract, pancreatitis, inflammatory bowel disorders, hypotension, hypovolaemia, raised intracranial pressure, intracranial lesions or head injury (due to risk of increased intracranial pressure), reduced level of consciousness of uncertain origin, seep apnoea,or patients taking benzodiazepines, other CNS depressants (including alcohol) or MAO inhibitors (see section *Drug interactions and incompatibilities*).

Opioids may cause sleep-related breathing disorders including central sleep apnoea (CSA) and sleep-related hypoxemia. Opioid use may increase the risk of CSA in a dose-dependent manner in some patients. Opioids may also cause worsening of pre-existing sleep apnoea (see section *Side effects*). In patients who present with CSA, consider decreasing the total opioid dosage.

Concomitant use of oxycodone and sedative medicines such as benzodiazepines or related drugs may result in sedation, respiratory depression, coma and death. Because of these risks, concomitant prescribing with these sedative medicines should be reserved for patients for whom alternative treatment options are not possible. If a decision is made to prescribe oxycodone concomitantly with sedative 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. In this respect, it is strongly recommended to inform patients and their caregivers to be aware of these symptoms.

OxyNorm® capsules must be administered with caution in patients taking MAOIs or who have received MAOIs within the previous two weeks.

OxyNorm® capsules should not be used where there is a possibility of paralytic ileus occurring. As with all opioid preparations, oxycodone products should be used with caution following 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, ***OxyNorm®*** capsules should be discontinued immediately. ***OxyNorm®*** capsules should be used with caution pre-operatively and within the first 12-24 hours post-operatively.

As with all opioid preparations, ***OxyNorm®*** capsules should be used with caution following abdominal surgery as opioids are known to impair intestinal motility and should not be used until the physician is assured of normal bowel function.

As with all opioid preparations, patients who are to undergo cordotomy or other pain relieving surgical procedures should not receive ***OxyNorm®*** capsules for 6 hours before surgery. If further treatment with oxycodone is indicated then the dosage should be adjusted to the new post-operative requirement.

For appropriate patients who suffer with chronic non-malignant pain, opioids should be used as part of a comprehensive treatment programme involving other medications and treatment modalities. A crucial part of the assessment of a patient with chronic non-malignant pain is the patient's addiction and substance abuse history.

If opioid treatment is considered appropriate for the patient, then the main aim of treatment is not to minimise the dose of opioid, but rather to achieve a dose which provides adequate pain relief with a minimum of side effects. There must be frequent contact between physician and patient so that dosage adjustments can be made. It is strongly recommended that the physician defines treatment outcomes in accordance with pain management guidelines. The physician and patient can then agree to discontinue treatment if these objectives are not met.

<u>Drug dependence, tolerance and potential for abuse</u>

For all patients, prolonged use of this product may lead to physical dependence (addiction), even at therapeutic doses. The risks are increased in individuals with current or past history of substance misuse disorder (including alcohol misuse) or mental health disorder (e.g. major depression).

Additional support and monitoring may be necessary when prescribing for patients at risk of opioid misuse.

A comprehensive patient history should be taken to document concomitant medications, including over-the-counter medicines and medicines obtained on-line, and past and present medical and psychiatric conditions.

Patients may find that treatment is less effective with chronic use and express a need to increase the dose to obtain the same level of pain control as initially experienced. Patients may also supplement their treatment with additional pain relievers. These could be signs that the patient is developing tolerance. The risks of developing tolerance should be explained to the patient.

Overuse or misuse may result in overdose and/or death. It is important that patients only use medicines that are prescribed for them at the dose they have been prescribed and do not give this medicine to anyone else.

Patients should be closely monitored for signs of misuse, abuse or addiction.

The clinical need for analgesic treatment should be reviewed regularly.

Drug withdrawal syndrome

Prior to starting treatment with any opioids, a discussion should be held with patients to put in place a withdrawal strategy for ending treatment with oxycodone.

Drug withdrawal syndrome may occur upon abrupt cessation of therapy or dose reduction. When a patient no longer requires therapy, it is advisable to taper the dose gradually to minimise symptoms of withdrawal. Tapering from a high dose may take weeks to months.

The opioid drug withdrawal syndrome is characterised by some or all of the following: restlessness, lacrimation, rhinorrhoea, yawning, perspiration, chills, myalgia, mydriasis and palpitations. Other symptoms may also develop including irritability, agitation, anxiety, hyperkinesia, tremor, weakness, insomnia, anorexia, abdominal cramps, nausea, vomiting, diarrhoea, increased blood pressure, increased respiratory rate or heart rate.

If women take this drug during pregnancy, there is a risk that their newborn infants will experience neonatal withdrawal syndrome.

Oxycodone has an abuse profile similar to other strong agonist opioids. Oxycodone may be sought and abused by people with latent or manifest addiction disorders.
There is potential for development of psychological dependence [addiction] to opioid analgesics, including oxycodone. ***OxyNorm®*** capsules should be used with particular care in patients with a history of alcohol and drug abuse

As with other opioids, infants who are born to dependent mothers may exhibit withdrawal symptoms and may have respiratory depression at birth.

Hyperalgesia

Hyperalgesia may be diagnosed if the patient on long-term opioid therapy presents with increased pain. This might be qualitatively and anatomically distinct from pain related to disease progression or to breakthrough pain resulting from development of opioid tolerance. Pain associated with hyperalgesia tends to be more diffuse than the pre-existing pain and less defined in quality. Symptoms of hyperalgesia may resolve with a reduction of opioid dose.

The capsules should be swallowed whole, and not chewed or crushed.

Abuse of oral dosage forms by parenteral administration can be expected to result in serious adverse events, such as local tissue necrosis, infection, pulmonary granulomas, increased risk of endocarditis, and valvular heart injury, which may be fatal.

Concomitant use of alcohol and ***OxyNorm®*** capsules may increase the undesirable effects of ***OxyNorm®*** capsules; concomitant use should be avoided.

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.

Use in chronic, non-malignant pain

The use of ***OxyNorm®*** capsules for the treatment of chronic pain which is not due to malignancy should be restricted to situations where:

- All other conservative methods of analgesia have been tried and have failed;
- The pain is having a significant impact on patient's quality of life;
- There is no pain psychological contraindication, drug seeking behaviour or history of drug misuse.

OxyNorm® capsules will generally be used in a short term trial to determine if the pain is opioid responsive (see Administration and Dosage). One doctor should be responsible for the prescription and monitoring of the patient's opioid use.

Special risk groups

Renal and hepatic impairment

In renal and hepatic impairment, the administration of ***OxyNorm®*** capsules 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 ⅓ to ½ of the usual dose with cautious titration.

Elderly

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

Elderly, debilitated patients

As with other opioid initiation and titration, doses in elderly patients who are debilitated should be reduced 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.

Carcinogenicity/Mutagenicity

Oxycodone was not mutagenic in the Ames *Salmonella* and *E.coli* assays, but was positive in the mouse lymphoma assay. In assays of chromosomal damage, genotoxic effects occurred in the human lymphocyte

chromosomal aberration assay *in vitro*, but not in the *in vivo* bone marrow micronucleus assay in mice. The data from these assays indicate that the genotoxic risk to humans may be considered low.

Studies of oxycodone in animals to evaluate its carcinogenic potential have not been conducted owing to the length of clinical experience with the drug substance.

Impairment of Fertility

Studies have not been performed to assess the effects of oxycodone on fertility.

Side effects

Immediate release formulations such as ***OxyNorm®*** capsules may have a higher incidence of some adverse reactions than controlled-release formulations such as ***OxyContin®*** tablets. Adverse drug reactions are typical of full opioid agonists, and tend to reduce with time, with the exception of constipation. Anticipation of adverse drug reactions and appropriate patient management can improve acceptability.

Immune system disorders	
Uncommon	Anaphylactic reaction, anaphylactoid reaction, hypersensitivity
Psychiatric disorders	
Common	Anxiety, depression, confusional state, insomnia, nervousness, thinking disturbances, abnormal dreams
Uncommon	Affect liability, agitation, depression, decreased libido, drug dependence, euphoria, hallucinations,disorientation, mood altered, restlessness, dysphoria
Eye disorders	
Uncommon	Miosis, visual disturbance
Ear and labyrinth disorders	
Uncommon	Vertigo, tinnitus
Hepato-biliary disorders	
Uncommon	Biliary colic, increased hepatic enzymes
Musculoskeletal and connective tissue disorders	
Uncommon	Muscular rigidity
Gastrointestinal	
Common	Constipation, nausea, vomiting, dry mouth, anorexia, hiccup, dyspepsia, abdominal pain & diarrhoea.
Uncommon	Colic, stomatitis, dysphagia, eructation, flatulence, gastrointestinal disorders, increased appetite, ileus & gastritis.
Nervous system disorders	
Common	Headache, faintness, dizziness, sedation, somnolence, twitching, tremor, lethargy
Uncommon	Drowsiness, convulsion, dysgeusia, raised intracranial pressure, hypothermia, abnormal gait, agitation, depression, tremor, amnesia, muscle contraction

Immune system disorders	
	involuntary, hyperkinesia, hypoaesthesia, hypertonia, hypotonia, paraesthesia, speech disorder, stupor seizures, taste perversion, syncope.
Genitourinary	
Uncommon	Ureteric spasm, urinary retention, erectile dysfunction, urinary abnormalities, urinary infection, amenorrhea and decreased libido.
Cardiac disorders	
Uncommon	Supraventricular tachycardia, bradycardia, ST depression & chest pain, palpitation (as part of withdrawal syndrome)
Vascular disorders	
Uncommon	Hypotension, , blood pressure and heart rate reductions, migraine, vasodilation, facial flushing, orthostatic hypotension.
Metabolic and Nutritional disorders	
Uncommon	Decreased appetite, Dehydration, oedema, hyponatraemia, peripheral oedema & thirst.
Respiratory disorders	
Common	Bronchospasm, dyspnoea, pharyngitis, voice alteration, cough decreased.
Uncommon	Respiratory depression, hiccups.
Dermatological disorders	
Common	Rash, pruritus, hyperhidrosis
Uncommon	Dry skin, exfoliative dermatitis, urticaria, angioedema and other skin rashes
General disorders and administration site conditions	
Common	Sweating, pruritus, , asthenia & chills.
Uncommon	Accidental injury, pain, neck pain, oedema, oedema peripheral, malaise, thirst, pyrexia, drug withdrawal syndrome , lymphadenopathy.

Key: ≥ 1 % Common , ≤ 1% Uncommon

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.

Effect on ability to drive and use machinery

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.

Administration and dosage

OxyNorm® capsules should be swallowed whole and not opened, chewed or crushed.

Non-malignant pain:

Opioids are not first-line therapy for chronic non-malignant pain nor are they recommended as the only treatment. Types of chronic pain which have been shown to be alleviated by strong opioids include chronic osteoarthritic pain and intervertebral disc disease. In common with other strong opioids, the need for continued treatment should be assessed at regular intervals.

Adults, elderly and children over 18 years:
Prior to initiation and titration of doses, refer to the **Warnings and Precautions** section for information on special risk groups such as females and the elderly.

OxyNorm® capsules 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.

Generally, the lowest effective dose for analgesia should be selected.
Increasing severity of pain will require an increased dosage of ***OxyNorm®*** capsules. 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 drug reactions prevent this.

OxyNorm® capsules 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 oxycodone preparation such as ***OxyContin®*** tablets, in accordance with the clinical guidelines on the use of opioid analgesics in such patients

The usual starting dose for opioid naive patients or patients presenting with severe pain uncontrolled by weaker opioids is 5 mg, 4-6 hourly. The dose should then be carefully titrated, as frequently as once a day if necessary, to achieve pain relief.

Prior to starting treatment with opioids, a discussion should be held with patients to put in place a strategy for ending treatment with oxycodone in order to minimise the risk of addiction and drug withdrawal syndrome (see section Warnings and precautions).

Conversion from oral morphine
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 emphasised that this is a guide to the dose of ***OxyNorm®*** capsules required. Inter-patient variability requires that each patient be carefully titrated to the appropriate dose.

Elderly patients
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 drug reactions were seen based on age therefore adult doses and dosage intervals are appropriate.

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. The recommended adult starting dose should be reduced by 50% (for example a total daily dose of 10 mg orally in opioid naïve patients), and each patient should be titrated to adequate pain control according to their clinical situation. The starting dose for opioid naïve patients is 2.5 mg oxycodone 6-hourly, given as ***OxyNorm®*** liquid**.**

Children under 18 years: OxyNorm® capsules should not be used in patients under 18 years.

*Multiplication Factors for Converting the Daily Dose of Prior Opioids to the Daily Dose of Oral Oxycodone**
(Mg/Day Prior Opioid x Factor = Mg/Day Oral Oxycodone)

	Oral Prior Parenteral	**Parenteral Opioid**
Oxycodone	1	--
Codeine	0.15	--
Hydromorphone	4	20
Pethidine (Meperidine)	0.1	0.4
Methadone	1.5	3
Morphine	0.5	3

* to be used for conversion to oral oxycodone. For patients receiving high-dose parenteral opioids, a more conservative conversion is warranted. For example, for high-dose parenteral morphine, use 1.5 instead of 3 as a multiplication factor.

Cessation of Therapy:

When a patient no longer requires therapy with oxycodone, it may be advisable to taper the dose gradually to prevent symptoms of withdrawal.

Overdosage

Symptoms: Acute overdosage with oxycodone can be manifested by miosis, respiratory depression, somnolence progressing to stupor or coma, skeletal muscle flaccidity, cold and clammy skin, constricted

pupils, hallucinations, bradycardia, hypotension, hypotonia, pulmonary oedema, circulatory failure and death.

Treatment of oxycodone overdosage: Primary attention should be given to the establishment of a patent airway and institution of assisted or controlled ventilation.

A saline cathartic or sorbitol added to the first dose of activated charcoal may speed gastrointestinal passage of the product. Administration of activated charcoal should be restricted to patients with an intact gag reflex or protected airway.
Oxygen, intravenous fluids, vasopressors and other supportive measures should be used as indicated.

If there are signs of clinically significant respiratory or cardiovascular depression, the use of an opioid antagonist should be considered. The opioid antagonist naloxone hydrochloride is a specific antidote against respiratory depression due to overdosage. Concomitant efforts at respiratory resuscitation should be carried out. The patient should be under continued surveillance and doses of the antagonist should be repeated as needed to maintain adequate respiration.

In an individual physically dependent on opioids, the administration of the usual dose of opioid antagonist will precipitate an acute withdrawal syndrome. The severity of this syndrome will depend on the degree of physical dependence and the dose of antagonist administered. The use of opioid antagonists in such individuals should be avoided if possible. If an opioid antagonist must be used to treat serious respiratory depression in the physically dependent patient, the antagonist should be administered with extreme care by using dosage titration, commencing with 10 to 20% of the usual recommended initial dose.

STORE DRUGS OUT OF CHILDREN'S REACH

Presentation
OxyNorm® capsules 5 mg (orange/beige), 10 mg (white/beige), 20 mg (pink/beige), in blister packs of 28 capsules (two blister stripes of 14 capsules).
Do not store above 30°C

Shelf life
36 months

Date of revision of the text
January 2021

Marketing Authorisation Holder
MUNDIPHARMA PHARMACEUTICALS PTE. LTD.
10 Marina Boulevard
#08-02 Marina Bay Financial Centre Tower 2
Singapore 018983

Manufactured by
BARD PHARMACEUTICALS LTD.
Cambridge Science Park
Milton Road
Cambridge CB4 0GW, UK.

®: OXYNORM and OXYCONTIN are Registered Trademarks.

9831-4