OxyNorm® oral solution 1mg/ml

Name of the Medicinal Product

OxyNorm® oral solution 1mg/ml

Qualitative and Quantitative Composition

Each ml of ***OxyNorm***® oral solution 1mg/ml contains oxycodone base 0.9 mg as oxycodone hydrochloride 1 mg. Excipient with known effect: Each ml ***OxyNorm***® oral solution 1mg/ml contains 1 mg sodium benzoate.

Pharmaceutical Form

OxyNorm® oral solution 1mg/ml is a clear colourless/straw-coloured solution.

Clinical Particulars
Therapeutic Indication

The management of acute exacerbation of moderate to severe chronic pain unresponsive to non-narcotic analgesia, and post-operative pain.

Posology and method of administration

Route of administration:
Oral

Post-operative pain:
In common with other strong opioids, the need for continued treatment should be assessed at regular intervals.

Elderly and adults over 18 years:
OxyNorm® oral solutions 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 ***OxyNorm***® oral solutions. 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® oral solutions 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 naïve 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. 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 emphasised that this is a guide to the dose of ***OxyNorm***® oral solutions required. Inter-patient variability requires that each patient is 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 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 (refer Special warnings and precautions for use).

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

Use in 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. The need for continued treatment in non-malignant pain should be assessed at regular intervals.

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.

Contraindications

Hypersensitivity to oxycodone or to any of the excipients listed in section '*Pharmaceutical Particulars'.* Oxycodone must not be used in any situation where opioids are contraindicated: severe respiratory depression with hypoxia, cor pulmonale, acute abdomen, severe chronic obstructive lung disease, cor pulmonale, elevated carbon dioxide levels in the blood, cardiac arrhythmias, severe bronchial asthma, chronic bronchial asthma or other chronic obstructive airways disease, elevated carbon dioxide levels in the blood, paralytic ileus, suspected surgical 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.

Special warnings and precautions for use

The primary risk of opioid excess is respiratory depression.

Sleep related breathing disorders

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 *Undesirable effects*). In patients who present with CSA, consider decreasing the total opioid dosage.

As with all narcotics, a reduction in dosage may be advisable in hypothyroidism, Addison's disease and myxedema. 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 myxoedema, hypothyroidism, Addison's disease, toxic psychosis, prostate 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, sleep apnoea or patients taking benzodiazepines, other CNS depressants (including alcohol) or MAO inhibitors (see *section Interaction with other medicinal products and other forms of interaction*).

Concomitant use of oxycodone and sedative medicines such as benzodiazepines or related drugs benzodiazepines and opioids may result in sedation, respiratory depression, coma and death. Because of these risks, concomitant prescribing with these sedative medicines of sedative medicines such as benzodiazepines or related drugs with opioids should be reserved for patients for whom alternative treatment options are not possible.

If a decision is made to prescribe benzodiazepines oxycodone concomitantly with opioids sedative medicines, the lowest effective dose should be used, and the duration of treatment should be as short as possible (see also general dose recommendation in section *Posology and method of administration*).

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 environment caregivers to be aware of these symptoms (see section *Interaction with other medicinal products and other forms of interaction*).

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

OxyNorm® oral solutions should not be used where there is a possibility of paralytic ileus occurring. Should paralytic ileus be suspected or occur during use, ***OxyNorm***® oral solutions should be discontinued immediately. ***OxyNorm***® oral solutions liquid should be used with caution pre-operatively and within the first 12-24 hours post-operatively. 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. Patients about to undergo additional pain relieving procedures (e.g. surgery, plexus blockade) should not receive***OxyNorm***® oral solutions for 6 hours prior to the intervention. 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. There is potential for development of psychological dependence (addiction) to opioid analgesics, including oxycodone. ***OxyNorm***® oral solutions like all opioids should be used with particular care in patients with a history of alcohol and drug abuse.

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>
Oxycodone has an abuse profile similar to other strong opioids. Oxycodone may be sought and abused by people with latent or manifest addiction disorders.

<u>Opioid Use Disorder (abuse and dependence)</u>
Tolerance and physical and/or psychological dependence may develop upon repeated administration of opioids such as oxycodone. Iatrogenic addiction following therapeutic use of opioids is known to occur.

Repeated use of ***OxyNorm*** oral solution may lead to Opioid Use Disorder (OUD). Abuse or intentional misuse of ***OxyNorm*** oral solution 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).

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

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.

<u>Tolerance</u>

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 with oxycodone, it is advisable to taper the dose gradually to prevent symptoms of withdrawal. Tapering from a high dose may take weeks to months. The opioid abstinence or withdrawal syndrome is characterised by some or all of the following: restlessness, lacrimation, rhinorrhoea, yawning, perspiration, chills, myalgia, mydriasis and palpitations. Other symptoms also may develop, including: irritability, anxiety, backache, joint pain, weakness, abdominal cramps, insomnia, nausea, anorexia, vomiting, diarrhoea, or increased blood pressure, 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. 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.

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

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.

OxyNorm® oral solutions contains 1 mg sodium benzoate in each ml. Sodium benzoate may increase jaundice in new-born babies (up to 4 weeks old).

This medicinal product contains 5.5 mg sodium per ml, equivalent to 0.275% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

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.

Oxycodone has an abuse profile similar to other strong opioids. Oxycodone may be sought and abused by people with latent or manifest addiction disorders

Elderly

The plasma concentrations of oxycodone are only nominally affected by age, being approximately 15% greater in elderly as compared to young subjects.

Elderly, debilitated patients

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

Renal and hepatic impairment

In renal and hepatic impairment, the administration of ***OxyNorm***® oral solutions 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 < 60 ml/min) or hepatic impairment should be reduced to 1/3 to ½ of the usual dose with cautious titration.

Interaction with other medicinal products and other forms of interaction

The concomitant use of sedative medicines such as benzodiazepines or related drugs such opioids with sedative medicines such as benzodiazepines or related drugs with opioids 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 *Special warnings and precautions for use*).

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 and alcohol.tranquillisers, anaesthetics, hypnotics, anti-depressants, non-benzodiazepine sedatives, phenothiazines, neuroleptic drugs, alcohol, other opioids, muscle relaxants and antihypertensives.

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.

MAO inhibitors are known to interact with narcotic analgesics, MAO-inhibitors cause CNS excitation or depression associated with hypertensive or hypotensive crisis (see section *Special warnings and precautions for use*). Co-administration with monoamine oxidase inhibitors or within two weeks of discontinuation of their use should be avoided.

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

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.

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.

CYP3A4 inducers, such as rifampicin, carbamazepine, phenytoin and St John´s Wort may induce the metabolism of oxycodone and cause an increased clearance of oxycodone that could cause a reduction of the plasma concentrations of oxycodone. The oxycodone dose may need to be adjusted accordingly.

Drugs 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 with a modified release oxycodone tablet resulted in an increase in oxycodone Cmax by 11%, AUC by 13%, and t½ elim. by 14%. Also an increase in noroxycodone level was observed, (Cmax by 50%; AUC by 85%, and t½ elim. by 42%). The pharmacodynamic effects of oxycodone were not altered.

Concurrent administration of quinidine, an inhibitor of cytochrome P450-2D6 with a modified release oxycodone tablet, resulted in an increase in oxycodone Cmax by 11%, AUC by 13%, and t½ elim. by 14%. Also an increase in noroxycodone level was observed, (Cmax by 50%, AUC by 85%, and t½ elim. by 42%). The pharmacodynamic effects of oxycodone were not altered. This interaction may be observed for other potent inhibitors of cytochrome P450-2D6 enzyme. Cimetidine and inhibitors of cytochrome P450-3A4 such as ketoconazole and erythromycin may inhibit the metabolism of oxycodone.

Fertility, pregnancy and lactation

Pregnancy

OxyNorm® oral solutions 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.

Breastfeeding

Administration to nursing women is not recommended as oxycodone may be secreted in breast milk and may cause respiratory depression in the infant.**Effects on ability to drive and use machines**

Oxycodone may impair the ability to drive and use machines. Oxycodone may modify patients' reactions to a varying extent depending on the dosage and individual susceptibility. Therefore, patients should not drive or operate machinery if affected.

Undesirable effects

Immediate release formulations such as ***OxyNorm®*** solutions 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. Tolerance and dependence may occur (see Tolerance and Dependence, below). Constipation may be prevented with an appropriate laxative. If nausea and vomiting are troublesome, oxycodone may be combined with an anti-emetic.

Common (incidence of≥ 1%) and uncommon (incidence of≤ 1%) adverse drug reactions are listed in the table below.

Body System	Common	Uncommon
Immune system disorders		Anaphylactic reaction Anaphylactoid reaction Hypersensitivity
Metabolism and nutritional disorders	Decreased appetite, Anorexia	Dehydration
Psychiatric disorders	Anxiety Confusional state Depression Insomnia Nervousness	Affect lability Agitation Depression Drug dependence Euphoric mood

	Abnormal thinking Abnormal dreams	Hallucinations Disorientation Mood altered Restlessness Dysphoria Decreased libido
Nervous system disorders	Headache Dizziness Sedation Somnolence Tremor	Amnesia Hypertonia Hypoaesthesia Hypotonia Paraesthesia Speech disorder Convulsions Muscle contractions involuntary Taste perversion Syncope
Eye disorders		Miosis Visual impairment
Ear and labyrinth disorders		Vertigo
Cardiac disorders		Supraventricular tachycardia
Vascular disorders		Hypotension Orthostatic hypotension Vasodilatation Facial flushing
Respiratory, thoracic and mediastinal disorders	Bronchospasm Dyspnoea Cough decreased	Respiratory depression Hiccups
Gastrointestinal disorders	Constipation Nausea Vomiting Dry mouth Dyspepsia Abdominal pain Diarrhoea	Dysphagia Eructation Flatulence Gastrointestinal disorders Ileus Gastritis
Hepato-biliary disorders		Biliary colic Increased hepatic enzymes
Skin and subcutaneous tissue disorders	Hyperhidrosis Pruritus Rash	Dry skin Exfoliative dermatitis Urticaria
Musculoskeletal and connective tissue disorders		Muscular rigidity

Renal and urinary disorders		Urinary retention Ureteral spasm
Reproductive system and breast disorders		Amenorrhoea Libido decreased Erectile dysfunction
General disorders and administration site conditions	Asthenia Chills Fatigue	Drug tolerance Oedema Oedema peripheral Malaise Thirst Pyrexia Drug withdrawal syndrome

Tolerance and Dependence:
The patient may develop tolerance to the drug with chronic use and require progressively higher doses to maintain pain control. Prolonged use of ***OxyNorm***® oral solutions may lead to physical dependence and a withdrawal syndrome may occur upon abrupt 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.
The opioid abstinence or withdrawal syndrome is characterised by some or all of the following: restlessness, lacrimation, rhinorrhoea, yawning, perspiration, chills, myalgia, mydriasis and palpitations. Other symptoms also may develop, including: irritability, anxiety, backache, joint pain, weakness, abdominal cramps, insomnia, nausea, anorexia, vomiting, diarrhoea, or increased blood pressure, respiratory rate or heart rate.

Overdose
Acute overdose with oxycodone can be manifested by miosis, respiratory depression and hypotension. Circulatory failure and somnolence progressing to stupor or deepening coma, skeletal muscle flaccidity, hypotonia, bradycardia, pulmonary oedema and death may occur in more severe cases.

Patients should be informed of the signs and symptoms of overdose and to ensure that family and friends are also aware of these signs and to seek immediate medical help if they occur.

Treatment of oxycodone overdosage:

Primary attention should be given to the establishment of a patent airway and institution of assisted or controlled ventilation. The pure opioid antagonists such as naloxone are specific antidotes against symptoms from opioid overdose. Other supportive measures should be employed as needed.

In the case of massive overdosage, administer naloxone intravenously (0.4 to 2 mg for an adult and 0.01 mg/kg body weight for children), if the patient is in a coma or respiratory depression is present. Repeat the dose at 2 minute intervals if there is no response. If repeated doses are required then an infusion of 60% of the initial dose per hour is a useful starting point. A solution of 10 mg made up in 50 ml dextrose

will produce 200 micrograms/ml for infusion using an IV pump (dose adjusted to the clinical response). Infusions are not a substitute for frequent review of the patient's clinical state. Intramuscular naloxone is an alternative in the event IV access is not possible. As the duration of action of naloxone is relatively short, the patient must be carefully monitored until spontaneous respiration is reliably re-established. Naloxone is a competitive antagonist and large doses (4 mg) may be required in seriously poisoned patients.

For less severe overdosage, administer naloxone 0.2 mg intravenously followed by increments of 0.1 mg every 2 minutes if required.

Naloxone should not be administered in the absence of clinically significant respiratory or circulatory depression secondary to oxycodone overdosage. Naloxone should be administered cautiously to persons who are known, or suspected, to be physically dependent on oxycodone. In such cases, an abrupt or complete reversal of opioid effects may precipitate pain and an acute withdrawal syndrome.

Additional/other considerations:

• Consider activated charcoal (50 g for adults, 10 -15 g for children), if a substantial amount has been ingested within 1 hour, provided the airway can be protected.

• Gastric contents may need to be emptied as this can be useful in removing unabsorbed drug.

Pharmacological Properties

Pharmacodynamic properties
Pharmacotherapeutic group: Natural opium alkaloids
ATC code: N02A A05

Oxycodone is a full opioid agonist with no antagonist properties. It has an affinity for kappa, mu and delta opiate receptors in the brain and spinal cord. Oxycodone is similar to morphine in its action. The therapeutic effect is mainly analgesic, anxiolytic and sedative.

Pharmacokinetic Properties

Compared with morphine, which has an absolute bioavailability of approximately 30%, oxycodone has a high absolute bioavailability of up to 87% following oral administration. Oxycodone has an elimination half life of approximately 3-4 hours and is metabolised principally to noroxycodone and oxymorphone. Oxymorphone has some analgesic activity but is present in the plasma at low concentrations and is not considered to contribute to oxycodone's pharmacological effect.

Limited data indicate that the 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.

A pharmacokinetic study in healthy volunteers has demonstrated that, following administration of a single 10 mg dose, ***OxyNorm***® oral solution 1mg/ml and ***OxyNorm***® concentrate oral solution 10mg/ml

provided an equivalent rate and extent of absorption of oxycodone. Mean peak plasma concentrations of approximately 20 ng/ml were achieved within 1.5 hours of administration, median tmax values from both strengths of oral solutions being less than one hour.

Studies involving controlled release oxycodone have demonstrated that the oral bioavailability of oxycodone is only slightly increased (16%) in the elderly.

In patients with renal and hepatic impairment, the bioavailability of oxycodone was increased by 60% and 90% respectively, and a reduced initial dose is recommended in these groups.

Preclinical safety data

Oxycodone was not mutagenic in the following assays: Ames Salmonella and E. Coli test with and without metabolic activation at doses of up to 5000 µg, chromosomal aberration test in human lymphocytes (in the absence of metabolic activation and with activation after 48 hours of exposure) at doses of up to 1500 µg/ml, and in the in vivo bone marrow micronucleus assay in mice (at plasma levels of up to 48 µg/ml). Mutagenic results occurred in the presence of metabolic activation in the human chromosomal aberration test (at greater than or equal to 1250 µg/ml) at 24 but not 48 hours of exposure and in the mouse lymphoma assay at doses of 50 µg/ml or greater with metabolic activation and at 400 µg/ml or greater without metabolic activation. The data from these tests 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.

Pharmaceutical Particulars
List of excipients
Saccharin sodium
Sodium benzoate
Citric acid monohydrate
Sodium citrate
Hydrochloric acid, dilute
Sodium hydroxide solution 5%w/v
Purified water

In addition, ***OxyNorm***® oral solution 1mg/ml contains Hypromellose 15mPa.s

Shelf life

48 months

Special precautions for storage

Do not store above 30 °C

STORE DRUGS OUT OF CHILDREN'S REACH

Nature and contents of container

OxyNorm® oral solution 1mg/ml is supplied in 100ml and 250 ml amber glass bottles with polyethylene/polypropylene screw caps.

Not all pack sizes and strengths are marketed locally.

Manufactured by:

Mundipharma Pharmaceuticals Limited
13 Othellos Street, Dhali Industrial Zone,
2540-Nicosia, Cyprus

Product Registrant:

Mundipharma Pharmaceuticals Pte Ltd
10 Marina Boulevard
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