OxyContin® tablets

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-methoxy17-methylmorphinan-6-one hydrochloride (CAS No: 124-90-3). The molecular formula is $C_{18}H_{21}NO_4$. HCl and molecular weight is 351.87.

The inactive ingredients in OxyContin® tablets are: lactose, povidone, Eudragit RS 30D (solids), glycerol triacetate, stearyl alcohol, talc and magnesium stearate. All of the tablets are coated with hypromellose, titanium dioxide and macrogol 400. The tablet coatings also contain: hydroxypropylcellulose (10 & 80 mg tablets); polysorbate 80 (20 & 40 mg tablets); iron oxide red CI77491 (20 mg tablets); iron oxide yellow CI77492 (40 & 80 mg tablets); indigo carmine CI73015 aluminium lake (80 mg tablets) and brilliant blue CI42090 (5 mg tablets).

Therapeutic properties

Oxycodone is a full opioid agonist with no antagonist properties whose principal therapeutic action is analgesia. 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. 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.

Absorption

Compared with morphine, which has an absolute bioavailability of approximately 30%, oxycodone has a high absolute bioavailability of up to 87% following oral administration.

The absorption of oxycodone from OxyContin® tablets is biphasic, with an initial absorption of approximately 40% of the active drug (T½ = 0.6 hrs) providing onset of analgesia within 1 hour in most patients, followed by a more controlled absorption, which determines the 12 hour duration of action (T½ = 6.2 hrs). The mean apparent half-life of OxyContin® tablets is 6.5 hours and steady-state is achieved in about one day. The initial absorption occurs from the surface of the tablet, following

dissolution of the film coat. The remaining drug substance is absorbed from the matrix either by dissolution or diffusion from or through the tablet matrix.

Release of oxycodone from OxyContin® tablets is independent of pH under physiological conditions.

OxyContin® tablets have an oral bioavailability comparable with conventional oral oxycodone, but achieve maximal plasma concentrations at about 3 hours compared with 1-1.5 hours for conventional oral oxycodone. Peak and trough concentrations of oxycodone from OxyContin® tablets 10 mg administered 12-hourly are similar to those achieved from conventional oxycodone 5 mg administered 6-hourly.

OxyContin® tablets 5 mg, 10 mg, 20 mg, 40 mg and 80 mg are dose-proportional in terms of both rate and extent of absorption. Ingestion of a standard high-fat meal does not alter the peak oxycodone concentration or the extent of oxycodone absorption from OxyContin® tablets.

Indication

The management of moderate to severe chronic pain unresponsive to non-narcotic analgesia.

Contraindications

Hypersensitivity to opioids and to any of the constituents or in any situation where opioids are contraindicated, acute respiratory depression , cor pulmonale, cardiac arrhythmias, severe bronchial asthma, chronic obstructive airways disease, , elevated carbon dioxide levels in the blood, paralytic ileus, suspected surgical abdomen, acute abdomen, severe constipation, moderate to severe hepatic impairment, severe renal impairment (creatinine clearance < 10ml/min) ,delayed gastric emptying, acute alcoholism, brain tumor, increased cerebrospinal or intracranial pressure, head injury, severe CNS depression, convulsive disorders, delirium tremens, hypercarbia, concurrent administration of monoamine oxidase inhibitors or within 2 weeks of discontinuation of their use. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine. Not recommended for pre-operative use or for the first 24 hours post-operatively. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Use in fertility, pregnancy and lactation

Pregnancy

Category C: Oxycodone, when used during labour, may cause respiratory depression in the new born, not recommended for use in pregnancy nor during labour. There are limited data from the use of oxycodone in pregnant women. Infants born to mothers who have received opioids during the last 3 to 4 weeks before giving birth should be monitored for respiratory depression. Withdrawal symptoms may be observed in the newborn of mothers undergoing treatment with oxycodone. Reproduction studies have been performed in rats and rabbits by oral administration at doses up to 8.0 mg/kg (48 mg/m^2) and 125.0 mg/kg (1375 mg/m^2), respectively, which are 0.4 and 11 times the human dose of 160 mg, based on Body Surface Area (BSA), respectively. The studies did not show evidence of harm to foetus. There are, however, no adequate and well controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human responses, this drug should be used during pregnancy only if clearly needed.

Breastfeeding

Low concentrations of oxycodone have been detected in breast milk. Oxycodone may be secreted in breast milk and may cause respiratory depression in the new born. Withdrawal symptoms can occur in breast-feeding infants when maternal administration of an opioid analgesic is stopped. OxyContin® tablets should not be used in breastfeeding mothers.

Drug interactions and incompatibility

Anticholinergic agents

Concurrent use with oxycodone may result in an increased risk of severe constipation and/or urinary retention.

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)

Non-selective MAOIs intensify the effects of opioid drugs 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 drug 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.

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.

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, antidepressants and inhibitors of P450-3A such as ketoconazole, voriconazole and erythromycin), 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.
The potential effects of oxycodone on CYP enzyme have not been studied either *in vitro* or *in vivo.*

Warnings and precautions
The major risk of opioid excess is respiratory depression. As with all opioids, a reduction in dosage may be advisable in hypothyroidism. Use with caution in opioid dependent patients and in patients with head injury (due to risk of increased intracranial pressure) or patients taking MAO inhibitors, , hypotension, hypovolaemia, diseases of the biliary tract, pancreatitis, inflammatory bowel disorders, Addison's disease, prostatic hypertrophy, adrenocortical insufficiency, toxic psychosis, chronic renal and hepatic disease, severe pulmonary disease, alcoholism, delirium tremens, and debilitated elderly and infirm patients. OxyContin® tablets should not be used where there is a possibility of paralytic ileus occurring. Should paralytic ileus be suspected or occur during use, OxyContin® tablets should be discontinued immediately. As with all opioid preparations, patients who are to undergo cordotomy or other pain relieving surgical procedures (e.g. surgery, plexus blockade) should not receive OxyContin® tablets for pre-operative use or within the first 12-24 hours postoperatively. Also, 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. Pain in the immediate preoperative period, and any symptoms of opioid withdrawal, should be managed with short-acting analgesic agents. If further treatment with OxyContin® tablets is then indicated the dosage should be adjusted to the new post-operative requirement.

OxyContin® 60 mg and 80 mg tablets should not be used in patients not previously exposed to opioids. These tablet strengths may cause fatal respiratory depression when administered to opioid naïve patients.

As with all opioid preparations, OxyContin® tablets 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.

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. OxyContin® tablets, like all opioids, should be avoided in patients with a history of, or present 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 minimum 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.

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

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

OxyContin® tablets must be swallowed whole, and not broken, chewed or crushed. The administration of broken, chewed or crushed OxyContin® tablets leads to rapid release and absorption of a potentially fatal dose of oxycodone (see Overdosage)

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

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

<u>Use in chronic, non-malignant pain</u>
The use of OxyContin® tablets 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 the patient's quality of life;

• there is no psychological contraindication, drug seeking behaviour or history of drug misuse.

Prior to long term prescription, a trial of OxyContin® tablets or shorter acting opioid should be undertaken. Long term administration of OxyContin® tablets should only occur if this trial demonstrates that the pain is opioid sensitive. Opioid naive patients who require rapid dose escalation with <u>no concomitant pain relief</u> within the trial period should generally be considered inappropriate for long term therapy.

One doctor only should be responsible for the prescription and monitoring of the patient's opioid use.

Prescribers should consult appropriate clinical guidelines on the use of opioid analgesics in such patients.

Drug dependence

As with other opioids, tolerance and physical dependence tend to develop upon repeated administration of oxycodone. There is potential for abuse of the drug and for development of strong psychological dependence. OxyContin® tablets should therefore be prescribed and handled with a high degree of caution appropriate to the use of a drug with strong abuse potential.

The patient may develop tolerance to the drug with chronic use and require progressively higher doses to maintain pain control. Prolonged use of this product 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.

Drug abuse is not, however, a problem in patients with severe pain in which oxycodone is appropriately indicated. On the other hand, in the absence of a clear indication for a strong opioid analgesic, drug-seeking behaviour must be suspected and resisted, particularly in individuals with a history of, or propensity for, drug abuse. Withdrawal symptoms may occur following abrupt discontinuation of oxycodone therapy or upon administration of an opioid antagonist. Therefore, patients on prolonged therapy should be withdrawn gradually from the drug if it is no longer required for pain control. Oxycodone should be used with caution and under close supervision in patients with pain not due to malignancy who have a prior history of substance abuse. However, in such cases, prior psychological assessment is essential and the prescribing doctor should consider whether the benefit of treatment outweighs the risk of abuse.

OxyContin® tablets consist of a dual-polymer matrix, intended for oral use only. Parenteral venous injection of the tablet constituents, especially talc, can be expected to result in local tissue necrosis, pulmonary granulomas and serious adverse reactions which may be fatal.

Special risk groups

Renal and hepatic impairment

In renal and hepatic impairment, the administration of OxyContin® tablets 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 $^{1}/_{3}$ 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 $^{1}/_{3}$ 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.

Studies of oxycodone in animals to evaluate its carcinogenic potential have not been conducted.

Impairment of Fertility

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

Side effects

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, confusional state, insomnia, nervousness, thinking abnormal, abnormal dreams
Uncommon	Affect lability, agitation, depression, drug dependence, euphoria, hallucinations, libido decreased, disorientation, mood altered, restlessness, dysphoria

Eye disorders	
Uncommon	Miosis, vision abnormal
Ear and labyrinth disorders	
Uncommon	Vertigo
Gastrointestinal disorders	
Common Uncommon	Constipation, nausea, vomiting, dry mouth, dyspepsia, abdominal pain & diarrhoea Colic, dental caries, stomatitis, dysphagia, eructation, flatulence, gastrointestinal disorders, increased appetite, ileus & gastritis
Hepato-biliary disorders	
Uncommon	Biliary colic, cholestasis, increased hepatic enzymes
Nervous System disorders	
Common Uncommon	Headache, asthenia, faintness, dizziness, sedation, somnolence & twitching, tremor, lethargy, sedation Drowsiness, convulsion, raised intracranial pressure, hypothermia, abnormal gait, tinnitus, muscle contractions involuntary, amnesia, hyperkinesia, hypoasthesia, hypertonia,hypotonia, malaise, paresthesia, speech disorder, taste perversion, syncope, stupor, euphoria, dysphoria, dysgeusia, seizures
Genitourinary disorders	
Uncommon	Biliary or ureteric spasm, water retention, urinary abnormalities, urinary tract infections, amenorrhea and erectile dysfunction, urinary retention, ureteral spasm
Cardiovascular disorders	
Uncommon	Palpitation as part of withdrawal syndrome,orthostatic hypotension, hypotension, bradycardia, blood pressure and heart rate reductions, syncope, migraine, vasodilation, ST depression & chest pain, flushing
Metabolic and Nutritional disorders	
Common Uncommon	Anorexia, decreased appetite Dehydration, hyponatraemia,
Respiratory, thoracic and mediastinal disorders	
Common Uncommon	Bronchospasm, dyspnoea, pharyngitis, voice alteration, cough decreased Respiratory depression, hiccups
Dermatological disorders	
Common Uncommon	Rash, hyperhidrosis, pruritus Dry skin, exfoliative dermatitis, urticaria, angioedema and other skin rashes
Musculoskeletal and connective tissue disorders	
Uncommon	Muscular rigidity
General disorders and administration site conditions	
Common	Sweating, pruritus, fever, chills , asthenia, fatigue

Uncommon	Accidental injury, pain, neck pain, miosis, muscular rigidity, lymphadenopathy, allergic reaction and anaphylactoid reactions, oedema, peripheral oedema & thirst, withdrawal syndrome (with or without seizures)
Reproductive system and breast disorder	
Common	Erectile dysfunction, hypogonadism
Hepato-biliary disorder	
Uncommon	Increased hepatic enzymes, biliary colic
Vascular disorder	
Uncommon	Vasodilation, facial flushing
Cardiac disorders	
Uncommon	Palpitations (in the context of withdrawal syndrome), supraventricular tachycardia

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 their ability is impaired, patients should not drive or operate machinery.

Administration and dosage
OxyContin® tablets 80 mg should only be used in opioid-tolerant patients.

OxyContin® tablets are to be swallowed whole, and are not to be broken, chewed or crushed. Taking broken, chewed or crushed OxyContin® tablets could lead to the rapid release and absorption of a potentially toxic dose of oxycodone.

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. OxyContin® tablets should be taken at 12-hourly intervals. The dosage is dependent on the severity of the pain, and the patient's previous history of analgesic requirements.

OxyContin® tablets are not intended for use as prn analgesic

Increasing severity of pain will require an increased dosage of OxyContin® tablets using individual tablet strengths, either alone or in combination, to achieve pain relief. The correct dosage for any individual patient is that which controls the pain and is well tolerated, for a full 12 hours. There is no ceiling dose and so patients should be titrated to pain relief unless unmanageable adverse drug reactions prevent

this. If higher doses are necessary, increases should be made, where possible, in 25% -50% increments. The need for escape medication more than twice a day indicates that the dosage of OxyContin® tablets should be increased.

The usual starting dose for opioid naive patients or patients presenting with severe pain uncontrolled by weaker opioids is 10 mg 12 hourly. The dose should then be carefully titrated, as frequently as once a day if necessary, to achieve pain relief. For the majority of patients, the maximum dose is 200 mg 12 hourly.

However, a few patients may require higher doses. Doses in excess of 1000 mg daily have been recorded.

Patients receiving oral morphine before OxyContin® tablets 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 OxyContin® tablets 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.

Children under 18 years: Not recommended.

Adults with mild to moderate renal impairment and mild hepatic impairment: The plasma concentration in this population may be increased. Therefore, dose initiation should follow a conservative approach. Patients should be started on OxyContin® tablets 5 mg 12 hourly or OxyNorm® liquid 2.5 mg 6 hourly and titrated to pain relief as described above.

Patients receiving other oral oxycodone formulation may be transferred to OxyContin® tablets at the same total daily dosage, equally divided into two 12-hourly OxyContin® tablet doses.

For patients who are receiving an alternative opioid, the “oral oxycodone equivalent” of the analgesic presently being used should be determined. Having determined the total daily dosage of the present analgesic, the following equivalence table can be used to calculate the approximate daily oral oxycodone dosage that should provide equivalent analgesia. The total daily oral oxycodone dosage should then be equally divided into two 12 hourly OxyContin® tablet doses.

*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 Opioid	**Parenteral Opioid**
Oxycodone	1	--
Codeine	0.15	--

Fentanyl TTS	SEE BELOW**	SEE BELOW**
Hydromorphone	4	20
Pethidine	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.

** Conversion from transdermal fentanyl to OxyContin® tablets: 18 hours following the removal of the transdermal fentanyl patch, OxyContin® tablets treatment can be initiated. Although there has been no systematic assessment of such conversion, a conservative oxycodone dose, approximately 10 mg q12h of OxyContin® tablets, should be initially substituted for each 25µg/hr fentanyl transdermal patch. The patient should be followed closely.

Use in non-malignant pain: Opiods 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.

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, bradycardia, hypotension, hypotonia, hallucinations, circulatory failure, pulmonary oedema and death may occur in more severe cases. The effects of overdosage will be potentiated by the simultaneous ingestion of alcohol or other psychotropic drugs.
Treatment of oxycodone overdosage: Primary attention should be given to the establishment of a patent airway and institution of assisted or controlled ventilation.

Administration of activated charcoal should be restricted to patients with an intact gag reflex or protected airway. A saline cathartic or sorbitol added to the first dose of activated charcoal may speed gastrointestinal passage of the product.

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. Since the duration of action of oxycodone, particularly sustained release

formulations, may exceed that of the antagonist, 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

OxyContin® tablets, 5 mg (pale blue), 10 mg (white), 20 mg (pink), 40 mg (yellow), 80 mg (green): blister packs of 28 tablets (two blister stripes of 14 tablets).

Not all strengths are available in all countries.

Do not store above 25°C

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