

Package leaflet: Information for the user
Oxycodone Hydrochloride 10mg/ml
Solution for Injection or Infusion
(referred to as Oxycodone Injection in this leaflet)

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, please ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Oxycodone Injection is and what it is used for
2. What you need to know before you use Oxycodone Injection
3. How to use Oxycodone Injection
4. Possible side effects
5. How to store Oxycodone Injection
6. Contents of the pack and other information

1. What Oxycodone Injection is and what it is used for

This injection has been prescribed for you by your doctor to relieve moderate to severe pain. It contains the active ingredient oxycodone which belongs to a group of medicines called strong analgesics or 'painkillers'.

2. What you need to know before you use Oxycodone Injection

Do not use Oxycodone injection if you:

- are allergic (hypersensitive) to oxycodone, or any of the other ingredients of the injection (listed in section 6);
- have breathing problems, such as severe chronic obstructive lung disease, severe bronchial asthma or severe respiratory depression. Your doctor will have told you if you have any of these conditions. Symptoms may include breathlessness, coughing or breathing more slowly or weakly than expected;
- have a condition where the small bowel does not work properly (paralytic ileus) or you have severe pain in your abdomen;
- have a heart problem after long-term lung disease (cor pulmonale);
- have moderate to severe liver problems. If you have other long-term liver problems you should only use this injection if recommended by your doctor;
- have ongoing problems with constipation;
- have elevated carbon dioxide levels in the blood.

Warnings and precautions

- Talk to your doctor, pharmacist or nurse before treatment with Oxycodone injection if you:
- are elderly or weakened;
 - have an under-active thyroid gland (hypothyroidism), as you may need a lower dose;
 - have myxoedema (a thyroid disorder with dryness, coldness and swelling ('puffiness') of the skin affecting the face and limbs);
 - have a head injury, severe headache or feel sick as this may indicate that the pressure in your skull is increased;
 - have low blood pressure (hypotension);
 - have low blood volume (hypovolaemia); this can happen with severe external or internal bleeding, severe burns, excessive sweating, severe diarrhoea or vomiting;
 - have a mental disorder as a result of an infection (toxic psychosis);
 - have inflammation of the pancreas (which causes severe pain in the abdomen and back);
 - have problems with your gall bladder or bile duct;
 - have inflammatory bowel disease;
 - have an enlarged prostate gland, which causes difficulty in passing urine (in men);
 - have poor adrenal gland function (your adrenal gland is not working properly which may cause symptoms including weakness, weight loss, dizziness, feeling or being sick), e.g. Addison's disease;
 - have breathing problems such as severe pulmonary disease. Your doctor will have told you if you have this condition. Symptoms may include breathlessness and coughing;
 - have kidney or liver problems;
 - have previously suffered from withdrawal symptoms such as agitation, anxiety, shaking or sweating upon stopping taking alcohol or drugs;
 - are or have ever been addicted to alcohol or drugs or have a known opioid dependence;
 - have an increased sensitivity to pain;
 - need to use increasingly higher doses of Oxycodone to gain the same level of pain relief (tolerance).

If you are going to have an operation, please tell the doctor at the hospital that you are using this medicine.

Children and adolescents

Do not give this medicine to children under 18 years the potential benefits are not greater than the risks.

Other medicines and Oxycodone injection

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. If you use this injection with some other medicines, the effect of this injection or the other medicines may be changed.

Tell your doctor or pharmacist if you are taking:

- a type of medicine known as a monoamine oxidase inhibitor or you have taken this type of medicine in the last two weeks;

- medicines to help you sleep or stay calm (for example tranquillisers, hypnotics or sedatives);
- medicines to treat depression (such as paroxetine);
- medicines to treat psychiatric or mental disorders (such as phenothiazines or neuroleptics);
- other strong analgesics ('painkillers');
- muscle relaxants;
- medicines to treat high blood pressure.
- quinine (a medicine to treat a fast heartbeat);
- cimetidine (a medicine for stomach ulcers, indigestion or heartburn);
- antifungal medicines (such as ketoconazole, voriconazole, itraconazole and posaconazole);
- antibiotics (such as clarithromycin, erythromycin or telithromycin);
- medicines known as 'protease inhibitors' to treat HIV (e.g. boceprevir, ritonavir, indinavir, nelfinavir or saquinavir);
- rifampicin (to treat tuberculosis);
- carbamazepine (a medicine treat seizures, fits or convulsions and certain pain conditions);
- phenytoin (a medicine to treat seizures, fits or convulsions);
- a herbal remedy called St. John's Wort (also known as *Hypericum perforatum*);
- antihistamines;
- medicines to treat Parkinson's disease.

Also tell your doctor if you have recently been given an anaesthetic.

Oxycodone Injection with food, drink and alcohol

Drinking alcohol during your treatment with this injection may make you sleepy or increase the risk of serious side effects such as shallow breathing with a risk of stopping breathing, and loss of consciousness. It is recommended not to drink alcohol while you're using Oxycodone injection.

You should avoid drinking grapefruit juice during your treatment with this medicine.

Pregnancy and breast-feeding

Do not use this injection if you are pregnant or breastfeeding.

Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machinery

This injection may cause a number of side effects such as drowsiness which could affect your ability to drive or use machinery (see section 4 for a full list of side effects).

These are usually most noticeable when you first start using the injection, or when changing to a higher dose. If you are affected you should not drive or use machinery.

This medicine can affect your ability to drive.

Do not drive whilst using this medicine until you know how this medicine affects you.

It may be an offence to drive if your ability to drive safely is affected. There is further information for patients who are intending to drive in Great Britain - go to: <http://www.gov.uk/drug-driving-law>

Talk to your doctor or pharmacist if you are not sure whether it is safe for you to drive while using this medicine.

Oxycodone Injection contains sodium

This medicinal product contains less than 1 mmol sodium (23 mg) per dose, i.e. essentially 'sodium-free'.

3. How to use Oxycodone Injection

A doctor or nurse will usually prepare and administer the injection for you. The injection should be used immediately after opening. The dose and how often the injection is given may be adjusted according to the severity of your pain.

Adults (over 18 years of age)

The recommended starting dose is dependent upon how the injection is administered. The recommended starting doses are as follows:

- As a single injection into a vein, the recommended dose is 1 to 10 mg given slowly over 1 to 2 minutes. This can be repeated every 4 hours.
- As an infusion into a vein, the recommended starting dose is 2 mg/hour.
- As a single injection through a fine needle into the tissue under the skin, the recommended starting dose is 5 mg repeated at 4-hourly intervals if needed.
- As an infusion through a fine needle into the tissue under the skin, the recommended starting dose is 7.5 mg/day.
- If given by patient controlled analgesia (PCA), the dose is worked out according to your weight (0.03 mg per kg of body weight). Your doctor or nurse will set a suitable frequency.

Use in children

Not to be used in patients under 18 years of age

Elderly

The lowest dose needed for symptom control should be used.



1. NAME OF THE MEDICINAL PRODUCT

Oxycodone Hydrochloride 10 mg/ml Solution for Injection or Infusion.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains oxycodone hydrochloride 10 mg (equivalent to 9 mg of oxycodone base). Each 1 ml ampoule contains oxycodone hydrochloride 10 mg (equivalent to 9 mg of oxycodone base).

Each 2 ml contains oxycodone hydrochloride 20 mg (equivalent to 18mg of oxycodone base). This medicinal product contains less than 1 mmol sodium (23 mg) per <dose>.

For full list of excipients, see Section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection or infusion (injection or infusion).

A clear, colourless solution practically free of particles.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For the treatment of moderate to severe pain in patients with cancer and post-operative pain.

For the treatment of severe pain requiring the use of a strong opioid.

4.2 Posology and method of administration

Route of administration

Subcutaneous injection or infusion.

Intravenous injection or infusion.

Posology:

The dose should be adjusted according to the severity of pain, the total condition of the patient and previous or concurrent medication.

Adults over 18 years:

The following starting doses are recommended. A gradual increase in dose may be required if analgesia is inadequate or if pain increases.

I.V. (Bulus): Dilute to 1 mg/ml in 0.9% saline, 5% dextrose or water for injections. Administer a bolus dose of 1 to 10 mg slowly over one to two minutes.

Doses should not be administered more frequently than every four hours.

I.V. (Infusion): Dilute to 1 mg/ml in 0.9% saline, 5% dextrose or water for injections. A starting dose of 2 mg/hour is recommended.

I.V. (PCA): Dilute to 1 mg/ml in 0.9% saline, 5% dextrose or water for injections. Bolus doses of 0.03 mg/kg should be administered with a minimum lock-out time of five minutes.

s.c. (Bulus): Use as 10 mg/ml concentration. A starting dose of 5 mg is recommended, repeated at four-hourly intervals as required.

s.c. (Infusion): Dilute in 0.9% saline, 5% dextrose or water for injections if required. A starting dose of 7.5 mg/day is recommended in opioid naive patients, titrating gradually according to symptom control. Cancer patients transferring from oral oxycodone may require much higher doses (see below).

Transferring patients between oral and parenteral oxycodone:

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

Elderly:

Elderly patients should be treated with caution. The lowest dose should be administered with careful titration to pain control.

Patients with renal and hepatic impairment:

Patients with mild to moderate renal impairment and/or mild hepatic impairment should be treated with caution. The lowest dose should be given with careful titration to pain control.

Children under 18 years:

There are no data on the use of Oxycodone injection in patients under 18 years of age.

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.

4.3 Contraindications

Hypersensitivity to oxycodone or to any of the excipients listed in section 6.1. Oxycodone must not be used in any situation where opioids are contraindicated, i.e. severe respiratory depression with hypoxia; paralytic ileus; acute abdomen; severe chronic obstructive lung disease; cor pulmonale; severe bronchial asthma; elevated carbon dioxide levels in the blood; moderate to severe hepatic impairment; chronic constipation.

4.4 Special warnings and precautions for use

The major risk of opioid excess is respiratory depression. Caution must be exercised when administering oxycodone to the debilitated elderly; patients with severely impaired pulmonary function, patients with impaired hepatic or renal function; patients with myxedema, 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, head injury (due to risk of increased intracranial pressure) or patients taking MAO inhibitors. Oxycodone injection should not be used where there is a possibility of paralytic ileus occurring. Should paralytic ileus be suspected or occur during use, Oxycodone injection should be discontinued immediately.

Oxycodone injection should be used with caution pre- or intra-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.

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 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.

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.

Hyperalgesia that will not respond to a further dose increase of oxycodone may occur, particularly in high doses. An oxycodone dose reduction or change to an alternative opioid may be required.

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. Oxycodone 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.

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

Oxycodone injection contains approximately 5mg sodium per ml i.e. essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

There can be an enhanced CNS depressant effect during concomitant therapy with drugs which affect the CNS such as tranquillisers, anaesthetics, hypnotics, antidepressants, sedatives, phenothiazines, neuroleptic drugs, alcohol, other opioids, muscle relaxants and antihypertensives.

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 4.4).

There should be a minimum 14 day MAO inhibitor washout period before initiating oxycodone therapy.

Alcohol may enhance the pharmacodynamic effects of Oxycodone, 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.

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.

Some specific examples are provided below:

- Itraconazole, a CYP3A4 inhibitor, administered 200 mg orally for five days, increased the AUC of oral oxycodone. On average, the AUC was approximately 1.8 times higher (range 1.3 – 2.3).
- Voriconazole, a CYP3A4 inhibitor, administered 200 mg twice-daily for four days (400 mg given as first two doses), increased the AUC of oral oxycodone. On average, the AUC was approximately 3.6 times higher (range 2.7 – 5.6).
- Telithromycin, a CYP3A4 inhibitor, administered 800 mg orally for four days, increased the AUC of oral oxycodone. On average, the AUC was approximately 1.8 times higher (range 1.3 – 2.3).
- Grapefruit Juice, a CYP3A4 inhibitor, administered as 200 ml three times a day for five days, increased the AUC of oral oxycodone. On average, the AUC was approximately 1.7 times higher (range 1.1 – 2.1).

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.

Some specific examples are provided below:

- St. John's Wort, a CYP3A4 inducer, administered as 300 mg three times a day for fifteen days, reduced the AUC of oral oxycodone. On average, the AUC was approximately 50% lower (range 37-57%).
- Rifampicin, a CYP3A4 inducer, administered as 600 mg once-daily for seven days, reduced the AUC of oral oxycodone. On average, the AUC was approximately 86% lower.

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.

4.6 Pregnancy and lactation

Pregnancy

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 pregnancy should be monitored for respiratory depression.

Withdrawal symptoms may be observed in the newborn of mothers undergoing treatment with oxycodone.

No studies on fertility or the post-natal effects of intrauterine exposure have been carried out. However, studies in rats and rabbits with oral doses of oxycodone equivalent to 3 and 47 times an adult dose of 160 mg/day, respectively, did not reveal evidence of harm to the foetus due to oxycodone. Oxycodone injection is not recommended for use in pregnancy nor during labour.

Breastfeeding

Oxycodone may be secreted in breast milk and may cause respiratory depression in the newborn. Oxycodone should therefore not be used in breast-feeding mothers.

4.7 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.

This medicine can impair cognitive function and can affect a patient's ability to drive safely. This class of medicine is in the list of drugs included in regulations under 5a of the Road Traffic Act 1988. When prescribing this medicine, patients should be told:

- The medicine is likely to affect your ability to drive
- Do not drive until you know how the medicine affects you
- It is an offence to drive while under the influence of this medicine
- However, you would not be committing an offence (called 'statutory defence') if:
 - o The medicine has been prescribed to treat a medical or dental problem and
 - o You have used it according to the instructions given by the prescriber and in the information provided with the medicine and
 - o It was not affecting your ability to drive safely

Details regarding a new driving offence concerning driving after drugs have been taken in the UK may be found here: <https://www.gov.uk/drug-driving-law>

4.8 Adverse drug effects

Adverse drug reactions are typical of full opioid agonists. Tolerance and dependence may occur (see 'Tolerance and Dependence', below). Constipation may be prevented with an appropriate laxative. If nausea or vomiting are troublesome, oxycodone may be combined with an antiemetic. The following frequency categories form the basis for classification of the undesirable effects:

Term	Frequency
Very common	≥ 1/10
Common	≥ 1/100 to <1/10
Uncommon	≥ 1/1,000 to <1/100
Rare	≥1/10,000 to <1/1,000
Very rare	<1/10,000
Frequency not known	Cannot be estimated from the available data

Immune system disorders:
Unknown: hypersensitivity.

Frequency not known: anaphylactic reaction, anaphylactoid reaction.

Metabolism and nutrition disorders:
Common: decreased appetite.

Unknown: dehydration.

Psychiatric disorders:
Common: anxiety, confusional state, depression, insomnia, nervousness, abnormal thinking, abnormal dreams

Patients with kidney or liver problems

Please tell your doctor if you suffer from kidney or liver problems as they may prescribe a lower dose depending on your condition. The dose recommended by the doctor should not be exceeded. Check with the doctor or pharmacist if you are unsure.
If you find that you are still in pain whilst being given this injection discuss this with your doctor.

If you use more Oxycodone injection than you should, or if someone else uses your injection

Call your doctor or hospital straight away. People who have been given an overdose may feel very sleepy, sick or dizzy. They may also have breathing difficulties leading to unconsciousness or even death and may need emergency treatment in hospital.
When seeking medical attention make sure that you take this leaflet and any remaining injection with you to show to the doctor.

If you stop using Oxycodone Injection

You should not suddenly stop using this injection unless your doctor tells you to.

If you want to stop using your injection, discuss this with your doctor first. They will tell you how to do this, usually by reducing the dose gradually so you do not experience unpleasant effects. Withdrawal symptoms such as agitation, anxiety, palpitations, shaking or sweating may occur if you suddenly stop using this injection.

If you have any further questions on the use of this injection, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, Oxycodone Injection can cause side effects, although not everybody gets them.
All medicines can cause allergic reactions, although serious allergic reactions are rare. **Tell your doctor immediately** if you get any sudden wheeziness, difficulties in breathing, swelling of the eyelids, face or lips, rash or itching especially those covering your whole body.

The most serious side effect is a condition where you breathe more slowly or weakly than expected (respiratory depression). **Tell your doctor immediately** if this happens to you.

As with all strong painkillers, there is a risk that you may become addicted or reliant on this injection.

Other possible side effects

Very common (May affect more than 1 in 10 people)

- Constipation (your doctor can prescribe a laxative to overcome this problem).
- Feeling or being sick (this should normally wear off after a few days, however your doctor can prescribe an anti-sickness medicine if it continues to be a problem).
- Drowsiness (this is most likely when you start using your medicine or when your dose is increased, but it should wear off after a few days).
- Dizziness.
- Headache.
- Itchy skin.

Common (May affect up to 1 in 10 people)

- Dry mouth, loss of appetite, indigestion, abdominal pain or discomfort, diarrhoea.
- Confusion, depression, a feeling of unusual weakness, shaking, lack of energy, tiredness, anxiety, nervousness, difficulty in sleeping, abnormal thoughts or dreams.
- Difficulty in breathing or wheezing, shortness of breath, decreased cough reflex.
- Rash.
- Sweating.

Uncommon (May affect up to 1 in 100 people)

- Difficulty in swallowing, belching, hiccups, wind, a condition where the bowel does not work properly (ileus), inflammation of the stomach, changes in taste.
- A feeling of dizziness or 'spinning', hallucinations, mood changes, unpleasant or uncomfortable mood, a feeling of extreme happiness, restlessness, agitation, generally feeling unwell, loss of memory, difficulty in speaking, reduced sensitivity to pain or touch, tingling or numbness in the hands or feet, seizures, fits or convulsions, blurred vision, fainting, unusual muscle stiffness or slackness, involuntary muscle contractions.
- Difficulty passing urine, impotence, decreased sexual drive, low levels of sex hormones in the blood ('hypogonadism', seen in a blood test).
- Fast, irregular heart beat, flushing of the skin.
- Dehydration, thirst, chills, swelling of the hands, ankles or feet.
- Dry skin, severe flaking or peeling of the skin.
- Redness of the face, reduction in size of the pupils in the eye, muscle spasm, high temperature.
- A need to use increasingly higher doses of this medicine to obtain the same level of pain relief (tolerance).
- Colicky abdominal pain or discomfort.
- A worsening of liver function tests (seen in a blood test)
- Drug withdrawal syndrome

Rare (May affect up to 1 in 1,000 people)

- Low blood pressure.
- A feeling of 'faintness' especially on standing up.
- Hives (nettle rash).

Not known (Frequency cannot be estimated from the available data)

- An increased sensitivity to pain.
- Aggression.
- Tooth decay.
- Absence of menstrual periods.
- A blockage in the flow of bile from the liver (cholestasis). This can cause itchy skin, yellow skin, very dark urine and very pale stools.
- Long term use of Oxycodone injection during pregnancy may cause life-threatening withdrawal symptoms in the newborn. Symptoms to look for in the baby include irritability, hyperactivity and abnormal sleep pattern, high pitched cry, shaking, being sick, diarrhoea and not putting on weight.

Unknown: agitation, affect lability, euphoric mood, hallucinations, decreased libido, drug dependence (see section 4.4), disorientation, mood altered, restlessness, dysphoria
Frequency not known: aggression.

Nervous system disorders:

Very common: somnolence, dizziness, headache.

Common: tremor, lethargy, sedation.

Unknown: amnesia, convulsion, hypertonia, hypoaesthesia, involuntary muscle contractions, speech disorder, syncope, paraesthesia, dysgeusia, hypotonia.

Frequency not known: hyperalgesia.

Eye disorders:

Unknown: visual impairment, miosis.

Ear and labyrinth disorders:

Unknown: vertigo.

Cardiac disorders:

Unknown: palpitations (in the context of withdrawal syndrome), supraventricular tachycardia.

Vascular disorders:

Unknown: vasodilatation, facial flushing.

Rare: hypotension, orthostatic hypotension.

Respiratory, thoracic and mediastinal disorders:

Common: dyspnoea, bronchospasm, cough decreased.

Unknown: respiratory depression, hiccups.

Gastrointestinal disorders:

Very common: constipation, nausea, vomiting.

Common: abdominal pain, diarrhoea, dry mouth, dyspepsia.

Unknown: dysphagia, flatulence, eructation, ileus, gastritis.

Frequency not known: dental caries.

Hepato-biliary disorders:

Unknown: increased hepatic enzymes, biliary colic.

Frequency not known: cholestasis.

Skin and subcutaneous tissue disorders:

Very common: pruritus.

Common: rash, hyperhidrosis.

Unknown: dry skin, exfoliative dermatitis.

Rare: urticaria.

Renal and urinary disorders:

Unknown: urinary retention, ureteral spasm.

Reproductive system and breast disorders:

Unknown: erectile dysfunction, hypogonadism.

Frequency not known: amenorrhoea.

General disorders and administration site conditions:

Common: asthenia, fatigue.

Unknown: drug withdrawal syndrome, malaise, oedema, peripheral oedema, drug tolerance, thirst, pyrexia, chills.

Frequency not known: drug withdrawal syndrome neonatal.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system:

United Kingdom

Yellow Card Scheme

www.mhra.gov.uk/yellowcard

Ireland

HPRA Pharmacovigilance

Earlsfort Terrace

IRL - Dublin 2

Tel: +353 1 6764971

Fax: +353 1 6762517

Website: www.hpra.ie

e-mail: medsafety@hpra.ie

Malta

ADR Reporting

www.medicinesauthority.gov.mt/adportal

4.9 Overdose

Symptoms of overdose

Acute overdose with oxycodone can be manifested by miosis, respiratory depression, hypotension and hallucinations. Nausea and vomiting are common in less severe cases.

Non-cardiac pulmonary oedema and rhabdomyolysis are particularly common after intravenous injection of opioid analgesics. Circulatory failure and somnolence progressing to stupor or coma, hypotonia, bradycardia, pulmonary oedema and death may occur in more severe cases.

The effects of overdose will be potentiated by the simultaneous ingestion of alcohol or other psychotropic drugs.

Treatment of overdose

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 overdose, administer naloxone intravenously (0.4 to 2mg for an adult and 0.01mg/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). It is not a substitute for frequent review of the patient's clinical state.

Intramuscular naloxone is an alternative in the event that 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 overdose, administer naloxone 0.2 mg intravenously followed by increments of 0.1 mg every 2 minutes if required.

The patient should be observed for at least 6 hours after the last dose of naloxone.

Naloxone should not be administered in the absence of clinically significant respiratory or circulatory depression secondary to oxycodone overdose. 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.

5. PHARMACOLOGICAL PROPERTIES

5.1 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 opioid receptors in the brain and spinal cord. Oxycodone is similar to morphine in its action. The therapeutic effect is mainly analgesic, anxiolytic, antitussive and sedative.

Gastrointestinal System

Opioids may induce spasm of the sphincter of Oddi.

Endocrine system

Opioids may influence the hypothalamic-pituitary-adrenal or gonadal axes. Some changes

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting systems listed below.

United Kingdom

Yellow Card Scheme

www.mhra.gov.uk/yellowcard

Ireland

HPRA Pharmacovigilance

Earlsfort Terrace

IRL - Dublin 2

Tel: +353 1 6764971

Fax: +353 1 6762517

Website: www.hpra.ie

e-mail: medsafety@hpra.ie

Malta

ADR Reporting

www.medicinesauthority.gov.mt/adportal

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Oxycodone Injection

Keep this medicine out of the sight and reach of children.

- This medicinal product does not require any special temperature storage conditions.
- Keep the ampoules in the outer carton in order to protect from light.
- Do not use after the expiry date (shown as Exp. on the packaging). The expiry date refers to the last day of the month, your doctor or nurse will check for this.
- This medicine should be used immediately after opening.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Oxycodone Injection contains

The active ingredient is oxycodone hydrochloride. Each ml contains oxycodone hydrochloride 10mg (equivalent to 9mg oxycodone base). Each 1 ml ampoule contains oxycodone hydrochloride 10 mg (equivalent to 9 mg of oxycodone base). Each 2 ml contains oxycodone hydrochloride 20 mg (equivalent to 18mg of oxycodone base).

The other ingredients are: citric acid monohydrate, sodium citrate, sodium chloride, hydrochloric acid, sodium hydroxide and water for injections.

What Oxycodone Injection looks like and the contents of the pack

Oxycodone Injection is a clear colourless solution and is supplied in packs of 5 containing either 1ml or 2ml clear glass ampoules.

Marketing Authorisation Holder: Wockhardt UK Ltd, Ash Road North, Wrexham, LL13 9UF, UK.

Manufacturer: CP Pharmaceuticals Ltd, Ash Road North, Wrexham, LL13 9UF, UK.

This medicinal product is authorised in the Member States of the EEA under the following names:

UK: Oxycodone Hydrochloride 10mg/ml Solution for Injection or Infusion

Ireland: Oxycodone Hydrochloride 10mg/ml Solution for Injection or Infusion

Cyprus: Oxycodone Hydrochloride 10mg/ml Solution for Injection or Infusion

Malta: Oxycodone Hydrochloride 10mg/ml Solution for Injection or Infusion

Poland: Oxycodone Hydrochloride Wockhardt

Other formats:



To listen to or request a copy of this leaflet in Braille, large print or audio please call, free of charge: 0800 198 5000 (UK Only). Please be ready to give the following information:

Product name	Reference number
Oxycodone 10mg/ml Solution for Injection	PL 29831/0359

This is a service provided by the Royal National Institute of Blind People. For the Republic of Ireland please call **UK +44 1978 669272**

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that can be seen include an increase in serum prolactin and decreases in plasma cortisol and testosterone. Clinical symptoms may be manifest from these hormonal changes.

Other pharmacological effects

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

5.2 Pharmacokinetic properties

Pharmacokinetic studies in healthy subjects demonstrated an equivalent availability of oxycodone from Oxycodone injection when administered by the intravenous and subcutaneous routes, as a single bolus dose or a continuous infusion over 8 hours.

Following absorption, oxycodone is distributed throughout the entire body. Approximately 45% is bound to plasma protein. It is metabolised in the liver to produce noroxycodone, oxymorphone and various conjugated glucuronides. The analgesic effects of the metabolites are clinically insignificant. The active drug and its metabolites are excreted in both urine and faeces. The plasma concentrations of oxycodone are only minimally affected by age, being 15% greater in elderly as compared to young subjects.

Female subjects have, on average, plasma oxycodone concentrations up to 25% higher than males on a body weight adjusted basis.

The drug penetrates the placenta and can be found in breast milk.

When compared to normal subjects, patients with mild to severe hepatic dysfunction may have higher plasma concentrations of oxycodone and noroxycodone, and lower plasma concentrations of oxymorphone. There may be an increase in the elimination half-life of oxycodone and this may be accompanied by an increase in drug effects.

When compared to normal subjects, patients with mild to severe renal dysfunction may have higher plasma concentrations of oxycodone and its metabolites. There may be an increase in the elimination half-life of oxycodone and this may be accompanied by an increase in drug effects.

5.3 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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Citric acid monohydrate
Sodium citrate
Sodium chloride
Hydrochloric acid (for pH adjustment)
Sodium hydroxide (for pH adjustment)
Water for injections

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

Cyclizine at concentrations of 3 mg/ml or less, when mixed with Oxycodone injection, either undiluted or diluted with water for injections, shows no sign of precipitation over a period of 24 hours storage at room temperature. Precipitation has been shown to occur in mixtures with Oxycodone injection at cyclizine concentrations greater than 3 mg/ml or when diluted with 0.9% saline. It is recommended that water for injections be used as a diluent when cyclizine and oxycodone hydrochloride are co-administered either intravenously or subcutaneously as an infusion. Prochlorperazine is chemically incompatible with Oxycodone injection.

6.3 Shelf life

Unopened 2 years.
The injection should be given immediately after opening the ampoule. Once opened, any unused portion should be discarded. Chemical and physical in-use stability has been demonstrated for 24 hours at room temperature.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8°C, unless reconstitution, dilution, etc has taken place in controlled and validated aseptic conditions.

6.4 Special precautions for storage

This medicinal product does not require any special temperature storage conditions.

Keep the ampoules in the outer carton in order to protect from light.

6.5 Nature and contents of container

Type I clear glass ampoules: 1 ml and 2 ml.

Pack size: 5 ampoules.

6.6 Special precautions for disposal and other handling

Oxycodone injection has been shown to be compatible with the following drugs:

Hyoscine butylbromide
Hyoscine hydrobromide
Dexamethasone sodium phosphate

Haloperidol
Midazolam hydrochloride
Metoclopramide hydrochloride
Levomepromazine hydrochloride

Oxycodone injection, undiluted or diluted to 1 mg/ml with 0.9% w/v saline, 5% w/v dextrose or water for injections, is physically and chemically stable when in contact with representative brands of polypropylene or polycarbonate syringes, polyethylene or PVC tubing, and PVC or EVA infusion bags, over a 24 hour period at room temperature.

The injection, whether undiluted or diluted to 1 mg/ml in the infusion fluids used in these studies and contained in the various assemblies, does not need to be protected from light.

Inappropriate handling of the undiluted solution after opening of the original ampoule, or of the diluted solutions may compromise the sterility of the product.

7. MARKETING AUTHORISATION HOLDER

Wockhardt UK Ltd

Ash Road North

Wrexham

LL13 9UF

UK

8. MARKETING AUTHORISATION NUMBER(S)

PL 29831/0359
PA 1339/25/1
MA 154/05/101

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Ireland: 16/07/2010

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10. DATE OF REVISION OF THE TEXT

12/2016

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