Package leaflet: Information for the user

Oxycodone Hydrochloride 10 mg/ml solution for injection/infusion
Oxycodone Hydrochloride 50 mg/ml solution for injection/infusion

Oxycodone hydrochloride

Read all of this leaflet carefully before you are given 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, 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 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'.

Oxycodone is indicated in adults only.

2. What you need to know before you use Oxycodone

Do not use Oxycodone:
- if you are allergic to oxycodone or any of the other ingredients of this medicine (listed in section 6);
- if you have known sensitivity to morphine or other opioids;
- 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 heart problem after long-term lung disease (cor pulmonale);
- have a condition where the small bowel does not work properly (paralytic ileus) or you have severe pain in your abdomen;
- have ongoing problems with constipation;
- are under 18 years of age.

Warnings and precautions
Talk to your doctor, pharmacist or nurse before treatment with Oxycodone 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 take 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 taking this medicine.

You may experience hormonal changes while taking this medicine. Your doctor may want to monitor these changes.

Other medicines and Oxycodone
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. This includes medicines obtained without a prescription. If you use this injection with some other medicines, the effect of this injection or the other medicines may be changed.

Concomitant use of opioids and benzodiazepines increases the risk of drowsiness, difficulties in breathing (respiratory depression), coma and may be life-threatening. Because of this, concomitant use should only be considered when other treatment options are not possible. However if your doctor does prescribe benzodiazepines or related drugs with opioids the dosage and duration of concomitant treatment should be limited by your doctor. Please follow your doctor's dosage recommendation closely. It could be helpful to inform friends or relatives to be aware of sign and symptoms stated above. Contact your doctor when experiencing such symptoms.

The risk of side effects increases, if you use antidepressants (such as citalopram, duloxetine, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline, venlafaxine). These medicines may interact with oxycodone and you may experience symptoms such as involuntary, rhythmic contractions of muscles, including the muscles that control movement of the eye, agitation, excessive sweating, tremor, exaggeration of reflexes, increased muscle tension, body temperature above 38°C. Contact your doctor when experiencing such symptoms.

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;
- quinidine (a medicine to treat a fast heart beat);
- 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 to 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 with drink and alcohol
Drinking alcohol during your treatment with Oxycodone 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 taking Oxycodone.
You should avoid drinking grapefruit juice during your treatment with this medicine.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before this medicine is administered to you.
There are limited data from the use of oxycodone in pregnant women. Prolonged use of oxycodone during pregnancy can cause withdrawal symptoms in newborns. Use of oxycodone during childbirth can cause breathing problems in the newborn.

Breast-feeding should be discontinued during treatment with Oxycodone. Oxycodone passes into breast milk and may affect your suckling child, especially following the intake of multiple doses.

Data concerning an influence of oxycodone on human fertility are not available.

Driving and using machines
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 as it may make you sleepy or dizzy.
- do not drive while taking this medicine until you know how it affects you
- it is an offence to drive if this medicine affects your ability to drive
- however, you would not be committing an offence if:
  - the medicine has been prescribed to treat a medical or dental problem and
  - you have taken it according to the instructions given by the prescriber or in the information provided with the medicine and
  - it was not affecting your ability to drive safely.

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

Oxycodone contains sodium
This medicinal product contains less than 1 mmol sodium (23 mg) per 1 ml, that is to say essentially "sodium-free".

3. How to use Oxycodone

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 usual starting dose is dependent upon how the injection is administered. The usual starting doses are as follows:
- As a single injection into a vein, the usual 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 usual starting dose is 2 mg/hour.
- As a single injection through a fine needle into the tissue under the skin, the usual 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 usual 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.

Children
Children and adolescents under 18 years of age should not be given the injection.

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 than you should
Call your doctor or hospital straight away. In severe cases an overdose may lead to unconsciousness or even death. 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 ampoules with you to show to the doctor.

If you stop using Oxycodone
You should not suddenly stop using this injection unless your doctor tells you to. If you want to stop using Oxycodone, 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 medicine, ask your doctor or nurse.

4. Possible side effects

Like all medicines, this medicine 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.

Very common side effects (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 taking your medicine or when your dose is increased, but it should wear off after a few days)
- dizziness
- headache
- itchy skin

Common side effects (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 side effects (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 heartbeat, 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 take 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)

Rare side effects (may affect up to 1 in 1 000 people)
- low blood pressure
- a feeling of 'faintness' especially on standing up
- hives (nettle rash)

Frequency 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 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

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via:
UK: Yellow Card Scheme, Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

IE: HPRA Pharmacovigilance, Earlsfort Terrace , IRL - Dublin 2, Tel: +353 1 6764971, Fax: +353 1 6762517, Website: www.hpra.ie, e-mail: medsafety@hpra.ie.

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

5. How to store Oxycodone

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

This medicinal product does not require any special storage conditions. Do not freeze.

Shelf life after first opening:
After opening, this medicinal product should be used immediately.

Shelf life after dilution:
Chemical and physical in-use stability has been demonstrated for 24 hours at 25°C and at 2-8°C (after dilution with sodium chloride 9 mg/ml (0.9%) solution for injection, 50 mg/ml (5%) dextrose or water for injections).
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 dilution has taken place in controlled and validated aseptic conditions.

Do not use this medicine if you notice any visible signs of deterioration (e.g. particles).

Do not use this medicine after the expiry date which is stated on the label and carton after {EXP}. The expiry date refers to the last day of that month.
Any unused portion should be discarded immediately.

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 contains
Oxycodone ***10 mg/ml***:
- The active substance is oxycodone hydrochloride.
  Each 1 ml ampoule contains 10 mg of oxycodone hydrochloride (equivalent to 9 mg of oxycodone).
  Each 2 ml ampoule contains 20 mg of oxycodone hydrochloride (equivalent to 18 mg of oxycodone).

Oxycodone ***50 mg/ml***:
- The active substance is oxycodone hydrochloride.
  Each 1 ml ampoule contains 50 mg of oxycodone hydrochloride (equivalent to 45 mg of oxycodone).

The other ingredients are citric acid monohydrate; sodium citrate, sodium chloride, sodium hydroxide (for pH adjustment), hydrochloric acid, concentrated (for pH adjustment), water for injections.

What Oxycodone looks like and contents of the pack
Clear, colourless solution for injection/infusion, free from visible particles.

Oxycodone is produced in 1 ml or 2 ml colourless glass ampoules.
Ampoules are marked with a specific colour ring code for each strength and volume.
Pack size:
5 or 10 ampoules of 1 ml
5 or 10 ampoules of 2 ml (only for 10 mg/ml)

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer
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This medicinal product is authorised in the Member States of the EEA under the following names:

Estonia	Oxycodone Kalceks
Germany	Oxycodon Ethypharm Kalceks 10 mg/ml Injektions-/Infusionslösung
	Oxycodon Ethypharm Kalceks 50 mg/ml Injektions-/Infusionslösung
Denmark	Oxycodone Kalceks
Finland	Oxycodone Kalceks
France	OXYCODONE KALCEKS 10 mg/mL, solution injectable/pour perfusion
	OXYCODONE KALCEKS 50 mg/mL, solution injectable/pour perfusion
Ireland	Oxycodone Hydrochloride 10 mg/ml, 50 mg/ml solution for injection/infusion
Lithuania	Oxycodone Kalceks 10 mg/ml, 50 mg/ml injekcinis ar infuzinis tirpalas
Latvia	Oxycodone Kalceks 10 mg/ml, 50 mg/ml šķīdums injekcijām/infūzijām
The Netherlands	Oxycodone Kalceks 10 mg/ml, 50 mg/ml oplossing voor injectie/infusie
Norway	Oxycodone Kalceks
Poland	Oxycodone Kalceks
Sweden	Oxycodone Kalceks
United Kingdom	Oxycodone Hydrochloride 10 mg/ml solution for injection/infusion
	Oxycodone Hydrochloride 50 mg/ml solution for injection/infusion

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The following information is intended for healthcare professionals only:

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 severity increases.

IV (Bolus): Dilute to 1 mg/ml in sodium chloride 9 mg/ml (0.9%) solution for injection, 50 mg/ml (5%) dextrose or water for injections. Administer a bolus dose of 1 to 10 mg slowly over 1-2 minutes. Doses should not be administered more frequently than every 4 hours.

IV (Infusion): Dilute to 1 mg/ml in sodium chloride 9 mg/ml (0.9%) solution for injection, 50 mg/ml (5%) dextrose or water for injections. A starting dose of 2 mg/hour is recommended.

IV (PCA): Dilute to 1 mg/ml in sodium chloride 9 mg/ml (0.9%) solution for injection, 50 mg/ml (5%) dextrose or water for injections. Bolus doses of 0.03 mg/kg should be administered with a minimum lock-out time of 5 minutes.

SC (Bolus): Use as 10 mg/ml concentration. Oxycodone 50 mg/ml dilute in sodium chloride 9 mg/ml (0.9%) solution for injection, 50 mg/ml (5%) dextrose or water for injections. A starting dose of 5 mg is recommended, repeated at 4-hourly intervals as required.

SC (Infusion): Dilute in sodium chloride 9 mg/ml (0.9%) solution for injection, 50 mg/ml (5%) dextrose or water for injections if required. A starting dose of 7.5 mg/day is recommended in opioid naïve 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. The patient should be monitored closely until stable when switching opioid medications.

Conversion of patients from IV morphine to IV oxycodone:
In patients who have received IV morphine prior treatment with IV oxycodone, the daily dosage should be based on 1:1 equivalence ratio. 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. The patient should be monitored closely until stable when switching opioid medications.

Elderly patients:
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:
The dose initiation should follow a conservative approach in these patients. The recommended adult starting dose should be reduced by 50% (for example a total daily dose of 10 mg orally in opioid naïve patients), and each patient should be titrated to adequate pain control according to their clinical situation.

Paediatric population:
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.

Endocrine system:
Opioids 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 be manifest from these hormonal changes.

Concomitant therapy
There can be an enhanced CNS depressant effect which can result in profound sedation, respiratory depression, coma and death during concomitant therapy with benzodiazepines or other drugs which affect the CNS such as tranquillisers, anaesthetics, hypnotics, antidepressants, non-benzodiazepine sedatives, phenothiazines, neuroleptic drugs, alcohol, other opioids, muscle relaxants and antihypertensives.

Duration of treatment:

Oxycodone should not be used for longer than necessary.

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

Route of administration
Subcutaneous injection or infusion.
Intravenous injection or infusion.

Incompatibilities
Cyclizine at concentrations of 3 mg/ml or less, when mixed with Oxycodone, 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 at cyclizine concentrations greater than 3 mg/ml or when diluted with sodium chloride 9 mg/ml (0.9%) solution for injection. However, if the dose of Oxycodone injection is reduced and the solution is sufficiently diluted with water for injections, concentrations greater than 3 mg/ml are possible. 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.

Instructions for use/handling
Each ampoule is for single use in a single patient. The medicinal product should be used immediately after opening the ampoule and any unused portion should be discarded.

Do not use if there are any visible signs of deterioration(e.g. particles).

Chemical and physical in-use stability has been demonstrated for 24 hours at 25°C and at 2-8°C. 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 dilution has taken place in controlled and validated aseptic conditions.

Oxycodone 10 mg/ml, undiluted or diluted to 1 mg/ml with sodium chloride 9 mg/ml (0.9%) solution for injection, 50 mg/ml (5%) dextrose or water for injections and Oxycodone 50 mg/ml, undiluted or diluted to 3 mg/ml with sodium chloride 9 mg/ml (0.9%) solution for injection, 50 mg/ml (5%) 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 (25 °C) and at 2-8°C. Oxycodone, whether undiluted or diluted in the infusion fluids used in these studies and contained in the various assemblies, does not need to be protected from light.
As well as product is compatible with following medicinal products: hyoscine butylbromide, hyoscine hydrobromide, dexamethasone sodium phosphate, haloperidol, midazolam hydrochloride, metoclopramide hydrochloride, levomepromazine hydrochloride, glycopyrronium bromide, ketamine hydrochloride.

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