Package leaflet: Information for the patient

Oxycodone hydrochloride/Naloxone hydrochloride 10 mg/5 mg

prolonged-release tablets

Oxycodone hydrochloride/Naloxone hydrochloride 20 mg/10 mg

prolonged-release tablets

Oxycodone hydrochloride/Naloxone hydrochloride 40 mg/20 mg

prolonged-release tablets

oxycodone hydrochloride/naloxone hydrochloride

Read all of this leaflet carefully before you start taking 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 or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

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1. What Oxycodone hydrochloride/Naloxone hydrochloride is and what it is used for

Oxycodone hydrochloride/Naloxone hydrochloride is a prolonged-release tablet, which means that its active substances are released over an extended period. Their action lasts for 12 hours.
These tablets are only for use in adults.

Pain relief
You have been prescribed Oxycodone hydrochloride/Naloxone hydrochloride for the treatment of severe pain, which can be adequately managed only with opioid analgesics. Naloxone hydrochloride is added to counteract constipation.

How these tablets work in pain relief
These tablets contain oxycodone hydrochloride and naloxone hydrochloride as active substances. Oxycodone hydrochloride is responsible for the painkilling effect of Oxycodone hydrochloride/Naloxone hydrochloride, and is a potent analgesic ("painkiller") of the opioid group.
The second active substance of Oxycodone hydrochloride/Naloxone hydrochloride, naloxone hydrochloride, is intended to counteract constipation. Bowel dysfunction (e.g. constipation) is a typical side effect of treatment with opioid painkillers.

2. What you need to know before you take Oxycodone hydrochloride/Naloxone hydrochloride

Do not take Oxycodone hydrochloride/Naloxone hydrochloride
- if you are allergic to oxycodone hydrochloride, naloxone hydrochloride, or any of the other ingredients of this medicine (listed in section 6);
- if your breathing is not able to supply enough oxygen to the blood, and get rid of carbon dioxide produced in the body (respiratory depression);
- if you suffer from a severe lung disease associated with narrowing of the airways (chronic obstructive pulmonary disease or COPD);
- if you suffer from a condition known as cor pulmonale. In this condition, the right side of the heart becomes enlarged, due to increased pressure inside blood vessels in the lung etc. (e.g. as a result of COPD – see above);
- if you suffer from severe bronchial asthma;
- if you have paralytic ileus (a type of bowel obstruction) not caused by opioids;
- if you have moderate to severe liver dysfunction.

Additionally for restless legs syndrome
- if you have a history of opioid abuse

Warnings and precautions
Talk to your doctor or pharmacist before taking Oxycodone hydrochloride/ Naloxone hydrochloride
- in the case of elderly patients or debilitated (weak) patients;
- if you have paralytic ileus (a type of bowel obstruction) caused by opioids;
- if you have kidney impairment;
- if you have mild liver impairment;
- if you have severe lung impairment(i.e. reduced breathing capacity);
- if you suffer with a condition characterised by frequent breathing stops during the night which may make you feel very sleepy during the daytime (sleep apnoea);
- if you have myxoedema (a thyroid disorder, with dryness, coldness and swelling ["puffiness"] of the skin, affecting the face and limbs);
- if your thyroid gland is not producing enough hormones (underactive thyroid or hypothyroidism);
- if your adrenal glands are not producing enough hormones (adrenal insufficiency or Addison's disease);
- if you have a mental illness accompanied by a (partial) loss of reality (psychosis), due to alcohol or intoxication with other substances (substance-induced psychosis);
- if you suffer from gallstone problems, or if you have any other biliary tract disorder (disease affecting the bile ducts, gallbladder etc.);
- if your prostate gland is abnormally enlarged (prostate hypertrophy);
- if you suffer from alcoholism or delirium tremens;
- if your pancreas is inflamed (pancreatitis);
- if you have low blood pressure (hypotension);
- if you have high blood pressure (hypertension);
- if you have pre-existing cardiovascular disease;
- if you have a head injury (due to the risk of increased brain pressure);
- if you suffer from epilepsy or are prone to seizures;
- if you are also taking MAO inhibitors (used to treat depression or Parkinson's disease), or you have taken this type of medicine in the last two weeks, e.g. medicines containing tranylcypromine, phenelzine, isocarboxazid, moclobemide and linezolid;
- if sleepiness or episodes of suddenly falling asleep occur.

Sleep-related breathing disorders
Oxycodone hydrochloride/Naloxone hydrochloride can cause sleep-related breathing disorders such as sleep apnoea (breathing pauses during sleep) and sleep related hypoxaemia (low oxygen level in the blood). The symptoms can include breathing pauses during sleep, night awakening due to shortness of breath, difficulties to maintain sleep or excessive drowsiness during the day. If you or another person observe these symptoms, contact your doctor. A dose reduction may be considered by your doctor.
Tell your doctor if any of the above has ever applied to you in the past. Also, please tell your doctor if you develop any of the above disorders while you are taking these tablets. The most serious result of opioid overdose is respiratory depression (slow and shallow breathing). This may also cause blood oxygen levels to fall, resulting in possible fainting, etc.

Opioid-induced ventilatory impairment and persistent post-operative opioid use
Do not use for acute post-operative pain owing to the increased risk of persistent post-operative opioid use (PPOU) and opioid-induced ventilatory impairment (OIVI).

You must swallow the prolonged-release tablet whole, so as not to affect the slow release of oxycodone hydrochloride from the prolonged-release tablet. Do not break, chew or crush the tablets. Taking broken, chewed or crushed tablets may lead to the absorption of a potentially lethal dose of oxycodone hydrochloride (see section 3: "If you take more Oxycodone hydrochloride/ Naloxone hydrochloride than you should").

If you experience severe diarrhoea at the start of treatment this may be due to the effect of naloxone. It may be a sign that bowel function is returning to normal. Such diarrhoea can occur within the first 3-5 days of treatment. If diarrhoea should persist after 3-5 days, or give you cause for concern, please contact your doctor.

If you have been using another opioid, withdrawal symptoms may occur when you initially switch to Oxycodone hydrochloride/Naloxone hydrochloride treatment, e.g. restlessness, bouts of sweating and muscle pain. If you experience such symptoms, you may need to be specially monitored by your doctor.

Tolerance, dependence and addiction
This medicine contains oxycodone which is an opioid medicine. Repeated use of opioid painkillers can result in the drug being less effective (you become accustomed to it, known as tolerance). Repeated use of Oxycodone hydrochloride/Naloxone hydrochloride can also lead to dependence, abuse, and addiction, which may result in life-threatening overdose. The risk of these side effects can increase with a higher dose and longer duration of use.

Dependence or addiction can make you feel that you are no longer in control of how much medicine you need to take or how often you need to take it. You might feel that you need to carry on taking your medicine, even when it doesn't help to relieve your pain.

The risk of becoming dependent or addicted varies from person to person. You may have a greater risk of becoming dependent or addicted on Oxycodone hydrochloride/Naloxone hydrochloride if:
- You or anyone in your family have ever abused or been dependent on alcohol, prescription medicines or illegal drugs ("addiction").
- You are a smoker.
- You have ever had problems with your mood (depression, anxiety or a personality disorder) or have been treated by a psychiatrist for other mental illnesses.

If you notice any of the following signs whilst taking Oxycodone hydrochloride/Naloxone hydrochloride, it could be a sign that you have become dependent or addicted.
- You need to take the medicine for longer than advised by your doctor
- You need to take more than the recommended dose
- You are using the medicine for reasons other than prescribed, for instance, 'to stay calm' of 'help you sleep'
- You have made repeated, unsuccessful attempts to quit or control the use of the medicine
- When you stop taking the medicine you feel unwell, and you feel better once taking the medicine again ('withdrawal effects').

If you notice any of these signs, speak to your doctor to discuss the best treatment pathway for you, including when it is appropriate to stop and how to stop safely (See section 3, If you stop taking Oxycodone hydrochloride/ Naloxone hydrochloride).

Contact your doctor if you experience severe upper abdominal pain possibly radiating to the back, nausea, vomiting or fever as this could be symptoms associated with inflammation of the pancreas (pancreatitis) or the biliary tract system.

Tell your doctor in case you have cancer associated to peritoneal metastases or beginning bowel obstruction in advanced stages of digestive and pelvic cancers.
If you need to undergo surgery, please tell your doctors that you are taking Oxycodone hydrochloride/Naloxone hydrochloride.

Similar to other opioids, oxycodone may affect the normal production of hormones in the body such as cortisol or sex hormones, particularly if you have taken high doses for long periods of time. If you experience symptoms which persist, such as feeling or being sick (including vomiting), loss of appetite, tiredness, weakness, dizziness, changes in menstrual cycle, impotence, infertility or decreased sex drive, talk to your doctor as he/she may want to monitor your hormone levels.

This medicine may increase your sensitivity to pain particularly at high doses. Tell your doctor if this happens. A reduction in your dose or a change in your medicine may be necessary.

You may notice remnants of the prolonged-release tablet in your stools. Do not be alarmed, as the active substances (oxycodone hydrochloride and naloxone hydrochloride) have already been released in the stomach and gut, and absorbed into your body.

Incorrect use of Oxycodone hydrochloride/Naloxone hydrochloride tablets

These tablets are not suitable for withdrawal treatment.

Oxycodone hydrochloride/Naloxone hydrochloride should never be abused, particularly if you have a drug addiction. If you are addicted to substances such as heroin, morphine or methadone, severe withdrawal symptoms are likely if you abuse these tablets because they contain the ingredient naloxone. Pre-existing withdrawal symptoms may be made worse.

You should never misuse these tablets by dissolving and injecting them (e.g. into a blood vessel). In particular, they contain talc, which can cause destruction of local tissue (necrosis) and changes in lung tissue (lung granuloma). Such abuse can also have other serious consequences and may even be fatal.

The use of Oxycodone hydrochloride/Naloxone hydrochloride may produce positive results in doping controls.

The use of Oxycodone hydrochloride/Naloxone hydrochloride as a doping agent may become a health hazard.

Other medicines and Oxycodone hydrochloride/Naloxone hydrochloride

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

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.

Concomitant use of opioids, including oxycodone hydrochloride and sedative medicines such as benzodiazepines or related drugs 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 Oxycodone hydrochloride/Naloxone hydrochloride together with sedative medicines the dose and duration of concomitant treatment should be limited by your doctor.

Please tell your doctor about all sedative medicines you are taking, and follow your doctor's dose recommendation closely. It could be helpful to inform friends or relatives to be aware of the signs and symptoms stated above. Contact your doctor when experiencing such symptoms. Examples of these sedatives or related medicines include:
- other potent painkillers (opioids);
- medicines to treat epilepsy, pain, and anxiety such as gabapentin and pregabalin;
- sleep medication and tranquilisers (sedatives including benzodiazepines, hypnotics, anxiolytics);
- medicines to treat depression;
- medicines used to treat allergies, travel sickness or nausea (antihistamines or antiemetics);
- medicines to treat psychiatric or mental disorders (antipsychotics which includes phenothiazines and neuroleptics);
- muscle relaxants;
- medicines to treat Parkinson's disease.

If you take these tablets at the same time as you take other medicines, the effect of these tablets or the other medicine as described below may be changed. Tell your doctor if you are taking:
- medicines that decrease the blood's clotting ability (coumarin derivatives), this clotting time may be speeded up or slowed down;
- antibiotics of the macrolide type (such as clarithromycin, erythromycin or telithromycin);
- antifungal medicines of the –azole type (such as ketoconazole, voriconazole, itraconazole or posaconazole);
- a specific type of medicine known as a protease inhibitor used to treat HIV (examples include ritonavir, indinavir, nelfinavir or saquinavir;
- cimetidine (a medicine for stomach ulcers, indigestion or heartburn);
- rifampicin (used to treat tuberculosis);
- carbamazepine (used to treat seizures, fits or convulsions and certain pain conditions);
- phenytoin (used to treat seizures, fits or convulsions);
- a herbal remedy called St John's Wort (also known as Hypericum perforatum);
- quinidine (a medicine to treat an irregular heartbeat).

No interactions are expected between Oxycodone hydrochloride/Naloxone hydrochloride and paracetamol, acetylsalicylic acid or naltrexone.

Oxycodone hydrochloride/Naloxone hydrochloride with food, drink and alcohol

Drinking alcohol whilst taking Oxycodone hydrochloride/Naloxone hydrochloride may make you feel more 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 hydrochloride/Naloxone hydrochloride. You should avoid drinking grapefruit juice while you are taking these tablets.

Pregnancy and breastfeeding

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Pregnancy

Use of these tablets should be avoided to the extent possible during pregnancy. If used over prolonged periods during pregnancy, oxycodone hydrochloride may lead to withdrawal symptoms in newborn infants. If oxycodone hydrochloride is given during childbirth, respiratory depression (slow and shallow breathing) may occur in the newborn infant.

Breastfeeding

Breastfeeding should be discontinued during treatment with these tablets. Oxycodone hydrochloride passes into breast milk. It is not known whether naloxone hydrochloride also passes into breast milk. Therefore, a risk for the suckling infant cannot be excluded in particular following intake of multiple doses of Oxycodone hydrochloride/Naloxone hydrochloride.

Driving and using machines

Oxycodone hydrochloride/Naloxone hydrochloride may affect your ability to drive or operate machines. In particular, this is likely at the start of Oxycodone hydrochloride/Naloxone hydrochloride therapy, after a dose increase or after switching from a different medication. However, these side effects disappear once you are on a stable Oxycodone hydrochloride/ Naloxone hydrochloride dose.

Oxycodone hydrochloride/Naloxone hydrochloride has been associated with sleepiness and episodes of suddenly falling asleep. If you experience these side effects, you must not drive or operate machinery. You should tell your doctor if this occurs.

The 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 hydrochloride/Naloxone hydrochloride contains lactose. This medicine contains lactose (milk sugar). If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking these tablets.

3. How to take Oxycodone hydrochloride/Naloxone hydrochloride

Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

Before starting treatment and regularly during treatment, your doctor will discuss with you what you may expect from using Oxycodone hydrochloride/ Naloxone hydrochloride, when and how long you need to take it, when to contact your doctor, and when you need to stop it (see also if you stop taking Oxycodone hydrochloride/Naloxone hydrochloride).

Oxycodone hydrochloride/Naloxone hydrochloride is a prolonged-release tablet, which means that its active substances are released over an extended period. Their action lasts for 12 hours.

You must swallow the prolonged-release tablet whole, so as not to affect the slow release of oxycodone hydrochloride from the prolonged-release tablet. Do not break, chew or crush the tablets. Taking broken, chewed or crushed tablets may lead to the absorption of a potentially lethal dose of oxycodone hydrochloride (see section 3 "If you take more Oxycodone hydrochloride/Naloxone hydrochloride than you should").

Unless otherwise prescribed by your doctor, the usual dose is:

To treat pain

Adults

The usual starting dose is 10 mg oxycodone hydrochloride / 5 mg naloxone hydrochloride as prolonged release tablet(s) every 12 hours.

Your doctor will decide how much you should take every day and how to divide your total daily dosage into morning and evening doses. Your doctor will also decide on any necessary dose adjustments during treatment. Your dose will be adjusted according to your level of pain and individual sensitivity. You should be given the lowest dose needed for pain relief. If you have already been treated with opioids, Oxycodone hydrochloride/Naloxone hydrochloride treatment can be started at a higher dose.

The maximum daily dose is 160 mg oxycodone hydrochloride and 80 mg naloxone hydrochloride. If you need a higher dose, your doctor may give you additional oxycodone hydrochloride without naloxone hydrochloride. However, the maximum daily dose of oxycodone hydrochloride should not exceed 400 mg.
The beneficial effect of naloxone hydrochloride on bowel activity may be affected if additional oxycodone hydrochloride is given without additional naloxone hydrochloride.

If you are switched from these tablets to another opioid pain medication, your bowel function will probably worsen.

If you experience pain between two doses of Oxycodone hydrochloride/ Naloxone hydrochloride, you may need a rapid-acting painkiller. Oxycodone hydrochloride/Naloxone hydrochloride is not suitable for this.

In this case, please talk to your doctor or pharmacist.

If you have the impression that the effect of these tablets is too strong or too weak, please talk to your doctor or pharmacist.

The maximum daily dose is 60 mg oxycodone hydrochloride and 30 mg naloxone hydrochloride.

Elderly patients

In general, no dose adjustment is necessary for elderly patients with normal kidney and/or liver function.

Liver or kidney impairment

If you have an impairment of your kidney function or a mild impairment of your liver function, your attending doctor will prescribe these tablets with special caution. If you have a moderate or severe impairment of liver function, these tablets should not be used (see also Section 2 'Do not take Oxycodone hydrochloride/Naloxone hydrochloride' and 'Warnings and Precautions').

Children and adolescents below 18 years of age

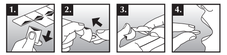
Oxycodone hydrochloride/Naloxone hydrochloride has not yet been studied in children and adolescents under 18 years of age. Its safety and effectiveness have not been proven in children and adolescents. For this reason, Oxycodone hydrochloride/Naloxone hydrochloride use in children and adolescents under 18 years of age is not recommended.

Method of administration

Oxycodone hydrochloride/Naloxone hydrochloride is for oral use.

Swallow these tablets whole (without chewing), with sufficient liquid (½ glass of water). You can take the prolonged-release tablets with or without food. Take the tablets every 12 hours, according to a fixed time schedule (e.g. at 8 o'clock in the morning and 8 o'clock in the evening). Do not break, chew or crush the prolonged-release tablets (see section 2 'Warnings and precautions').

Oxycodone hydrochloride/Naloxone hydrochloride is provided in perforated unit dose child-resistant peel-off blister. Remove a prolonged-release tablet from the package as follows:



1. Hold the blister at the edges and separate one cell from the rest of the blister by gently tearing along the perforations around it.
2. Pull up the edge of the foil and peel the foil off completely.
3. Tip the prolonged-release tablet out into your hand.
4. Swallow the whole prolonged-release tablet with sufficient liquid, with or without food.

Duration of use

In general, you should not take these tablets for any longer than you need to. If you are on long-term treatment, your doctor should regularly check whether you still need these tablets.

If you take more Oxycodone hydrochloride/Naloxone hydrochloride than you should

If you have taken more than the prescribed dose of these tablets, you must inform your doctor immediately.
An overdose may result in:
- narrowed pupils;
- slow and shallow breathing (respiratory depression);
- drowsiness up to loss of consciousness;
- low muscle tone (hypotonia);
- reduced pulse rate;
- a drop in blood pressure;
- a brain disorder (known as toxic leukoencephalopathy).

In severe cases, loss of consciousness (coma), fluid on the lungs and circulatory collapse may occur, which may be fatal in some cases.

You should avoid situations which require a high level of alertness, e.g. driving.

If you forget to take Oxycodone hydrochloride/Naloxone hydrochloride
Or if you take a dose lower than the one prescribed, you may not feel any effect.
If you forget to take your dose, please follow the instructions below:
- If your next usual dose is due in 8 hours or more: Take the forgotten dose immediately and continue with your normal dosing schedule.
- If your next usual dose is due within less than 8 hours: Take the forgotten dose. Then, wait another 8 hours before taking your next dose. Try to get back on track with your original dosing schedule (e.g. 8 o'clock in the morning and 8 o'clock in the evening). Do not take more than one dose within any 8-hour period.

Do not take a double dose to make up for a forgotten dose.

If you stop taking Oxycodone hydrochloride/Naloxone hydrochloride

Do not stop your treatment without consulting your doctor. If you do not require any further treatment, you must reduce the daily dose gradually after talking to your doctor. In this way, you will avoid withdrawal symptoms, such as restlessness, bouts of sweating and muscle pain.

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

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Important side effects to look out for, and what to do if you are affected:

If you are affected by any of the following important side effects, consult your nearest doctor immediately.
Slow and shallow breathing (respiratory depression) is the main danger of an opioid overdose. It mostly occurs in elderly and debilitated (weak) patients. Opioids can also cause a severe drop in blood pressure in susceptible patients.

<u>The following side effects have been seen in patients being treated for pain</u>

Common (may effect up to 1 in 10 people)
- abdominal pain
- constipation
- diarrhoea
- dry mouth
- indigestion
- vomit (be sick)
- feel sick
- flatulence (wind)
- decreased appetite up to loss of appetite
- a feeling of dizziness or 'spinning'
- headache
- hot flushes
- a feeling of unusual weakness
- tiredness or exhaustion
- itchy skin
- skin reactions/rash
- sweating
- vertigo
- difficulty in sleeping
- drowsiness

Uncommon (may affect up to 1 in 100 people)
- abdominal bloating
- abnormal thoughts
- anxiety
- confusion
- depression
- nervousness
- chest tightness, especially if you already have coronary heart disease
- drop in blood pressure
- withdrawal symptoms such as agitation
- fainting
- lack of energy
- thirst
- altered taste
- palpitations
- biliary colic
- chest pain
- generally feeling unwell
- pain
- swelling of hands, ankles or feet
- difficulties to concentrate
- impaired speaking
- shaking
- difficulties breathing
- restlessness
- chills
- hepatic enzymes increased
- rise in blood pressure
- reduced sexual drive
- runny nose
- cough
- hypersensitivity/allergic reactions
- weight loss
- injuries from accidents
- increased urge to urinate
- muscle cramps
- muscle twitches
- muscle pain
- vision impairment
- epileptic seizures (especially in persons with epileptic disorder or predisposition to seizures)

Rare (may affect up to 1 in 1,000 people)
- increase in pulse rate
- drug dependence
- dental changes
- weight gain
- yawning

Not known (frequency cannot be estimated from the available data)
- aggression
- euphoric mood
- severe drowsiness
- erectile dysfunction
- nightmares
- hallucinations
- shallow breathing
- difficulties in passing urine
- tingling skin (pins and needles)
- belching
- sleep apnoea (breathing pauses during sleep)

The active substance oxycodone hydrochloride, if not combined with naloxone hydrochloride, is known to have the following differing side effects:

Oxycodone can cause breathing problems (respiratory depression), reduction in size of the pupil in the eye, cramping of the bronchial muscles and cramping of the smooth muscles, as well as depression of the cough reflex.
Common (may affect up to 1 in 10 people)
- altered mood and personality changes (e.g. depression, feeling of extreme happiness)
- decreased activity
- increased activity
- difficulties in passing urine
- hiccups

Uncommon (may affect up to 1 in 100 people)
- impaired concentration
- migraines
- increased muscle tension
- involuntary muscle contractions
- a condition where the bowel stops working properly (ileus)
- dry skin
- drug tolerance
- reduced sensitivity to pain or touch
- abnormal coordination
- vocal changes (dysphonia)
- water retention
- difficulty in hearing
- mouth ulcers
- difficulties in swallowing
- sore gums
- perception disturbances (e.g. hallucination, derealisation)
- flushing of skin
- dehydration
- agitation
- a decrease in sex hormone levels which may affect sperm production in men or the menstrual cycle in female

Rare (may affect up to 1 in 1,000 people)
- itching rash (urticaria)
- infections such as cold sores or herpes (which may cause blisters around the mouth or genital area)
- increased appetite
- black (tarry) stools
- bleeding gums

Not known (frequency cannot be estimated from the available data)
- acute generalized allergic reactions (anaphylactic reactions)
- an increase in sensitivity to pain
- absence of menstrual periods
- withdrawal symptoms in the newborn
- problems with bile flow: a problem affecting a valve in the intestines that may cause severe upper abdominal pain (sphincter of Oddi dysfunction)
- tooth decay

The following side effects have been seen in patients being treated for restless legs syndrome

Very common (may affect 1 in 10 people or more)
- headache
- drowsiness
- constipation
- feel sick
- sweating
- tiredness or exhaustion

Common (may affect up to 1 in 10 people)
- decreased appetite to loss of appetite
- difficulty in sleeping
- depression
- a feeling of dizziness or 'spinning
- difficulties to concentrate
- shaking
- tingling in hands or feet
- vision impairment
- vertigo
- hot flushes
- drop in blood pressure
- rise in blood pressure
- abdominal pain
- dry mouth
- vomit (be sick)
- hepatic enzymes increased (alanine aminotransferase increased, gamma-glutamyltransferase increased)
- itchy skin
- skin reactions/rash
- chest pain
- chills
- pain
- thirst

Uncommon (may affect up to 1 in 100 people)
- reduced sexual drive
- episodes of suddenly falling asleep
- altered taste
- difficulties breathing
- wind
- erectile dysfunction
- withdrawal symptoms such as agitation
- swelling of hands, ankles or feet
- injuries from accidents

Not known (frequency cannot be estimated from available data)
- hypersensitivity/ allergic reactions
- abnormal thoughts
- anxiety
- confusion
- nervousness
- restlessness
- euphoric mood
- hallucinations
- nightmares
- epileptic seizures (especially in persons with epileptic disorder or predisposition to seizures)
- drug dependence
- severe drowsiness
- impaired speaking
- fainting
- chest tightness especially if you already have coronary heart disease
- palpitations
- increase in pulse rate
- shallow breathing
- cough
- runny nose
- yawning
- abdominal bloating
- diarrhoea
- aggression
- indigestion
- belching
- dental changes
- biliary colic
- muscle cramps
- muscle twitches
- muscle pain
- difficulties in passing urine
- increased urge to urinate
- generally feeling unwell
- weight loss
- weight increase
- a feeling of unusual weakness
- lack of energy

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 Yellow Card Scheme, Website: yellowcard.mhra.gov.uk or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Oxycodone hydrochloride/Naloxone hydrochloride

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

Do not use this medicine after the expiry date which is stated on the packaging after EXP. The expiry date refers to the last day of that month.

Do not store above 30ºC.
Store in the original package in order to protect from moisture.

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 hydrochloride/Naloxone hydrochloride contains
- The active substances are oxycodone hydrochloride and naloxone hydrochloride.
  <u>10 mg/5 mg prolonged-release tablets:</u>
  Each prolonged-release tablet contains 10 mg of oxycodone hydrochloride equivalent to 9 mg oxycodone and 5 mg naloxone hydrochloride as 5.45 mg naloxone hydrochloride dihydrate, equivalent to 4.5 mg naloxone.
  <u>20 mg/10 mg prolonged-release tablets:</u>
  Each prolonged-release tablet contains 20 mg of oxycodone hydrochloride equivalent to 18 mg oxycodone and 10 mg naloxone hydrochloride as 10.9 mg naloxone hydrochloride dihydrate, equivalent to 9 mg naloxone.
  <u>40 mg/20 mg prolonged-release tablets:</u>
  Each prolonged-release tablet contains 40 mg of oxycodone hydrochloride equivalent to 36 mg oxycodone and 20 mg naloxone hydrochloride as 21.8 mg naloxone hydrochloride dihydrate, equivalent to 18 mg naloxone.
- The other ingredients are:
  <u>10 mg/5 mg prolonged-release tablets:</u>
  hydroxypropylcellulose, ethylcellulose, glycerol distearate, lactose monohydrate, talc (E553b), magnesium stearate (E470b) in the tablet core and poly(vinyl alcohol), titanium dioxide (E171), macrogol 3350, talc (E553b) in film coating. See section 2 "Oxycodone hydrochloride/Naloxone hydrochloride contains lactose".
  <u>20 mg/10 mg prolonged-release tablets:</u>
  hydroxypropylcellulose, ethylcellulose, glycerol distearate, lactose monohydrate, talc (E553b), magnesium stearate (E470b) in the tablet core and poly(vinyl alcohol), titanium dioxide (E171), macrogol 3350, talc (E553b), red iron oxide (E172) in film coating. See section 2 "Oxycodone hydrochloride/Naloxone hydrochloride contains lactose".
  <u>40 mg/20 mg prolonged-release tablets:</u>
  hydroxypropylcellulose, ethylcellulose, glycerol distearate, lactose monohydrate, talc (E553b), magnesium stearate (E470b) in the tablet core and poly(vinyl alcohol), titanium dioxide (E171), macrogol 3350, talc (E553b), yellow iron oxide (E172) in film coating. See section 2 "Oxycodone hydrochloride/Naloxone hydrochloride contains lactose".

What Oxycodone hydrochloride/Naloxone hydrochloride looks like and contents of the pack
<u>10 mg/5 mg prolonged-release tablets:</u>
White, oval, slightly biconvex, film coated prolonged-release tablets engraved with "10" on one side of the tablet (dimensions: 9.5 mm x 4.5 mm).
<u>20 mg/10 mg prolonged-release tablets:</u>
Light pink, oval, slightly biconvex, film coated prolonged-release tablets engraved with "20" on one side of the tablet (dimensions: 9.5 mm x 4.5 mm).
<u>40 mg/20 mg prolonged-release tablets:</u>
Brownish yellow, capsule shaped, slightly biconvex, film coated prolonged-release tablets engraved with "40" on one side of the tablet (dimensions: 14.0 mm x 6.0 mm).

Oxycodone hydrochloride/Naloxone hydrochloride 10 mg/5 mg is available in packs containing 10, 14, 20, 28, 30, 50, 56, 60, 90, 98, 100 or 112 prolonged-release tablets in child-resistant blisters.
Oxycodone hydrochloride/Naloxone hydrochloride 20 mg/10 mg is available in packs containing 10, 20, 28, 30, 50, 56, 60, 90, 98, 100 or 112 prolonged-release tablets in child-resistant blisters.
Oxycodone hydrochloride/Naloxone hydrochloride 40 mg/20 mg is available in packs containing 10, 20, 28, 30, 50, 56, 60, 90, 98, 100 or 112 prolonged-release tablets in child-resistant blisters.

<u>Only for perforated unit dose child-resistant peel-off blisters:</u>
Oxycodone hydrochloride/Naloxone hydrochloride 10 mg/5 mg is available in packs containing 10 x 1, 14 x 1, 20 x 1, 28 x 1, 30 x 1, 50 x 1, 56 x 1, 60 x 1, 90 x 1, 98 x 1, 100 x 1 or 112 x 1 prolonged-release tablet in perforated unit dose child-resistant peel-off blisters.
Oxycodone hydrochloride/Naloxone hydrochloride 20 mg/10 mg is available in packs containing 10 x 1, 20 x 1, 28 x 1, 30 x 1, 50 x 1, 56 x 1, 60 x 1, 90 x 1, 98 x 1, 100 x 1 or 112 x 1 prolonged-release tablet in perforated unit dose child-resistant peel-off blisters.
Oxycodone hydrochloride/Naloxone hydrochloride 40 mg/20 mg is available in packs containing 10 x 1, 20 x 1, 28 x 1, 30 x 1, 50 x 1, 56 x 1, 60 x 1, 90 x 1, 98 x 1, 100 x 1 or 112 x 1 prolonged-release tablet in perforated unit dose child-resistant peel-off blisters.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer
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KRKA