Package leaflet: Information for the patient

Lindoxa 10 mg/ml solution for injection/infusion

oxycodone 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

1. What Lindoxa is and what it is used for

Lindoxa contains the active substance oxycodone hydrochloride which belongs to a group of medicines called opioids and has a strong analgesic (painkilling) effect.

Lindoxa is used to treat severe pain in adults (18 years and older), which requires treatment with an opioid analgesics because other painkillers have not been effective.

2. What you need to know before you are treated with Lindoxa

You must not be treated with Lindoxa
- if you are allergic to oxycodone hydrochloride or any of the other ingredients of this medicine (listed in section 6).
- if you have breathing problems, such as breathing more slowly or more weakly than expected (respiratory depression), low amount of oxygen (hypoxia) or too much carbon dioxide (hypercapnia) in your blood.
- if you have a severe chronic lung disease associated with narrowing of the airways (COPD = chronic obstructive pulmonary disease).
- if you have a certain heart condition after long-term lung disease known as cor pulmonale.
- if you have severe bronchial asthma.
- if you have a type of bowel obstruction called paralytic ileus.

Warnings and precautions
Talk to your doctor or pharmacist before using Lindoxa
- if you are elderly or debilitated (weak).
- if your lung, liver or kidney function is impaired.
- if you suffer from sleep apnoea (a condition where your breathing stops for short periods whilst you are asleep).
- if you have an impaired function of the thyroid gland (hypothyroidism or myxoedema).
- if you have poor adrenal gland function (your adrenal gland is not working properly) for example Addison’s disease.

- if you have a mental disorder called toxic psychosis as a result of intoxication with another substance or alcohol.
- if you or anyone in your family have ever abused or been dependent on alcohol, prescription medicines or illegal drugs ("addiction").
- if you are a smoker.
- if 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 have delirium tremens due to alcohol withdrawal causing severe confusion, hallucinations and shaking.
- if you have enlargement of the prostate.
- if you have an inflammation of the pancreas (pancreatitis) which may cause severe pain in the abdomen and back.
- if you have problems with your gall bladder or bile duct.
- If you have colicky abdominal pain or discomfort.
- if you have inflammatory bowel disease or suffer from constipation.
- if your brain pressure is increased e.g. as a result of a head injury.
- if you have low blood pressure or if you have a reduced blood volume.
- if you are taking medicines that affect the way the brain works (see section 2 "Other medicines and Lindoxa").
- if you are also taking a type of medicine known as MAO inhibitors (generally used to for the treatment of depression or Parkinson's disease) or if you have been taking them within the last 2 weeks.

Sleep-related breathing disorders
Lindoxa can cause sleep-related breathing disorders such as sleep apnoea (breathing pauses during sleep) and sleep related hypoxemia (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.

Lindoxa may supress the cough reflex.

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

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) and the biliary tract system.

Tolerance, dependence and addiction

This medicine contains oxycodone, which is an opioid. It can cause dependence and/or 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). This means, that you may need a higher dose to achieve the desired pain relief. Repeated use of Lindoxa 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 Lindoxa 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 Lindoxa, 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' or '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 Lindoxa).

Lindoxa has a dependence potential. If the treatment is stopped too suddenly, withdrawal symptoms may occur. If you no longer need treatment, your doctor will gradually reduce your daily dose.
Your doctor will weigh the possible risks against the expected and needs to be evaluated in relation to the benefit. Ask your doctor if you have any questions about this.

Increased sensitivity to pain that does not respond to dose increases can rarely develop. If this happens, your doctor will reduce your dose or switch you to an alternative opioid painkiller.

Children and adolescents
Use in children and adolescents below 18 years is not recommended.

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

The risk of side effects is increased if you take Lindoxa at the same time as medicines which affect the way the brain works. For example, you may feel very sleepy, or ***any*** breathing problems may get worse.

<u>Medicines that affect the way the brain works include:</u>
- other strong pain killers (opioids)
- medicines used to treat epilepsy, pain and anxiety (e.g. gabapentinoids such as pregabalin)
- sleeping pills and tranquillisers
- muscle relaxants
- medicines to treat depression
- medicines used to treat allergies, travel sickness or nausea (antihistamines or antiemetics)
- other medicines to treat psychiatric or mental disorders (phenothiazines, neuroleptics)
- medicines used to treat depression and Parkinson's disease (so-called MAO inhibitors, see also section 'Warnings and precautions')

Concomitant use of Lindoxa 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 Lindoxa 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.

Further interactions may occur with:
- cimetidine (used to manage excess of gastric acid)
- medicines that make your blood thinner, e.g. warfarin (so-called coumarin anticoagulants)
- quinidine (a medicine to treat a fast heart beat)
- medicines known as 'protease inhibitors' to treat HIV
- rifampicin (to treat tuberculosis)
- certain antibiotics (so-called macrolide anitbiotics) and antifungal medicines
- medicines to treat epilepsy (carbamazepine, phenytoin)
- St. John's Wort

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.

Lindoxa with drink and alcohol
Lindoxa should not be taken with alcohol. Alcohol use could increase serious side-effects of oxycodone, such as sleepiness and drowsiness and slow and shallow breathing.

Grapefruit juice may increase the levels of Lindoxa in your blood. Check with your doctor if you drink grapefruit juice regularly.

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 taking this medicine.

Pregnancy
The use of Lindoxa should be avoided to the extent possible during pregnancy.
Prolonged use of oxycodone during pregnancy can cause withdrawal symptoms in newborns. If oxycodone is given during childbirth it may cause berathing difficulties in the newborn.

Breast-feeding
Do not take this medicine if you are breast-feeding. Oxycodone passes into breast milk and may cause breathing difficulty in the baby.

Driving and using machines
Lindoxa may impair alertness and reactivity to such an extent that you may no longer be able to drive or operate tools and machines.

Ask your doctor whether you may drive or operate machines.

Lindoxa contains sodium chloride
This medicine contains less than 1 mmol sodium (23 mg) per ampoule, that is to say essentially 'sodium-free'.

3. How you are given Lindoxa

Always use this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure. A doctor or nurse will usually prepare and administer the injection for you.

Before starting treatment and regularly during treatment, your doctor will discuss with you what you may expect from using Lindoxa, 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 Lindoxa).

Adults (18 years and older)

Your doctor will adjust your dosage according to pain intensity and to your individual needs.
If you have been treated with other strong pain killers (opioids) before, the doctor may adjust your dose taking into account your previous dose.

If you experience pain between doses of Lindoxa you may require higher doses of Lindoxa. Please talk to your doctor if you have this problem.

You should not be given Lindoxa for longer than necessary.

How Lindoxa is given to you
Lindoxa is given as a single injection or slow infusion into vein or under the skin. It is given by a healthcare professional. In special cases Lindoxa can be given in patient-controlled analgesia. In such cases the doctor will instruct you how much and when to take Lindoxa.

If you use more Lindoxa than you should
Lindoxa is given to you by a doctor or nurse and is it not likely that you get too much. However if you believe you have gotten an too high dose, inform the hospital staff immediately.

In special cases Lindoxa may be given by yourself or a carer: if you think you have gotten too much of Lindoxa or if someone else has taken it by mistake, immediately contact a doctor, hospital or your local poison control center (<phone number>).

Symptoms of overdose are: a reduction in the size of the pupils, breathing problems, feeling weak in the muscles (low muscle tone), and a fall in blood pressure. In severe cases drowsiness or fainting due to a failure of the circulatory system (circulatory collapse), impairment of thinking and of movement, loss of consciousness (coma), reduced pulse rate and accumulation of fluid in the lungs may occur.
An overdose may result in a brain disorder (known as toxic leukoencephalopathy). Use of large amounts of Lindoxa may result in death.

If you forget to take Lindoxa
If you get a smaller dose of Lindoxa than prescribed, or if you miss a dose, adequate pain relief will probably not be achieved.

In special cases Lindoxa may be given by yourself or a carer:
If you forget to take one dose, you can take the forgotten dose as soon as you remember it.
Doses should not be administered more frequently than every 4 hours.

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

If you stop taking Lindoxa
Do not stop treatment without first speaking with your doctor as withdrawal symptoms may occur.

If you do not require treatment with Lindoxa anymore, your doctor will advise you on how to reduce the dose gradually to prevent the occurrence of withdrawal symptoms.

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.

Contact a doctor immediately if the following symptom occurs:
- **Very slow or weak breathing** (respiratory depression). This is the most most serious risk in connection with medicines such as Lindoxa (opioids), and may even be fatal after high doses of this medicine.

Other side effects that may occur:

Very common: may affect more than 1 in 10 people
- Sleepyness to drowsiness, sedation, dizziness, headache
- Constipation, feeling or being sick. Your doctor will prescribe an appropriate medicine to treat these symptoms.
- Itching

Common: may affect up to 1 in 10 people
- Changes in mood (anxiety, euphoric mood, confusion, depression, nervousness, sleep disorders, abnormal thoughts or dreams)
- Trembling
- Shortness of breath
- Reduction in the size of the pupils
- Widening of the blood vessels causing low blood pressure, fall in blood pressure on standing up which causes dizziness, light-headedness or fainting
- Dry mouth, rarely accompanied by thirst and difficulty swallowing, general symptoms of indigestion such as stomachache, diarrhoea, heartburn, decreased appetite
- Rash
- Sweating (sometimes heavily), fatigue, chills
- Weakness, tired, sleepiness
- Increase in the amount of a certain hormone (ADH = antidiuretic hormone) in the blood

Uncommon: may affect up to 1 in 100 people
- Allergic reactions
- Lack of water in the body (dehydration)
- Restlessness, mood swings, hallucinations, dysphoric mood, decreased libido, drug dependence
- Amnesia
- Tingling or numbness (e.g. in the hands or feet)
- Convulsions, increased or decreased muscle tension, or uncontrollled movements
- Reduced sensitivity to pain or touch
- Changes in taste
- Difficult speeking
- Visual impairment, visual disturbances
- Fainting or feeling of spinning or whirling (vertigo)
- Unpleasant sensation of irregular and/or forceful beating of the heart (in the context of withdrawal), increased pulse rate, low blood pressure
- Narrowing of the airways causing difficulty in breathing
- Difficulty swallowing, flatulence (excessive gas in the stomach or bowel), belching, obstruction of the bowel (ileus)
- Increased blood levels of certain hepatic enzymes (seen in blood tests), spasms in bililary tract
- Dry skin, itchy rash
- Problems passing urine, frequent urination and spasms
- Impotence, decreased hormone production in the testis/ovaries (hypogonadism)
- Feeling sick, fluid retention (oedema), thirst, physical dependence with withdrawal symptoms, tolerance

Rare: may affect up to 1 in 1,000 people

- Seizures (fits), in particular in patients having epilepsy or with a tendency to seizures
- Blood in urine
- Changes in body weight (loss or rise)

Not known: frequency cannot be estimated from the available data
- Severe allergic reactions (which may cause difficulty in breathing, dizziness, skin rashes, fever)
- Aggression
- Increased sensitivity to pain
- Sleep apnoea (breathing pauses during sleep)
- Cavities or tooth decay
- Painful conditions where bile cannot flow from the liver to the duodenum (cholestasis) or stomach pain due to a gallstone temporarily blocking the bile duct (biliary colic)
- A problem affecting a valve in the intestines that may cause severe upper abdominal pain (sphincter of Oddi dysfunction)
- Absence of menstrual bleeding
- Long term use of Lindoxa during pregnancy may cause life-threatening withdrawal symptoms in the new-born. 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 of the 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 the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Lindoxa

Keep this medicine out of the sight and reach of children. Store this medicine in a locked safe and secure storage space, where other people cannot access it. It can cause serious harm and be fatal to people when it has not been prescribed for them.

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

Do not freeze.

Once the ampoule is opened the solution for injection/infusion should be used immediately. Any unused solution should be discarded. Chemical and physical in-use stability has been demonstrated for 48 hours/days at room temperature.

This medicinal product is for single use only.

Only clear solution free from particles and discoloration should be used.

Do not throw away 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 Lindoxa contains

- The active substance is oxycodone hydrochloride. Each ml contains 10 mg oxycodone hydrochloride.

- The other ingredients are sodium chloride, citric acid monohydrate, sodium hydroxide (for pH-adjusting), hydrochloric acid (for pH-adjusting), water for injections.

What Lindoxa looks like and contents of the pack

Lindoxa is a clear, colourless to slightly yellowish solution.

Lindoxa is available in clear, colourless glass ampoules of 1 ml or 2 ml with OPC (one point cut) breaking system.
Lindoxa is packed in card board fold boxes containing 1, 3, 5 or 10 ampoules per pack.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

[To be completed nationally]

This medicinal product is authorised in the Member States of the EEA under the following names:
<to be completed>

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Detailed information on this medicine is available on the website of [name of MS agency (link)].

The following information is intended for healthcare professionals only:

Posology

The dosage depends on the pain intensity, the total condition of the patient, previous or concurrent medication, the patient's individual susceptibility to the treatment, body weight, and sex (higher plasma concentrations in females).

The following general dosage recommendations apply:

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

Adults (≥ 18 years of age)
i.v. (Bolus): 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 1-2 minutes to opioid-naïve patients.
Doses should not be administered more frequently than every 4 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 in opioid-naïve patients.

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 5 minutes to opioid-naïve patients.

s.c. (Bolus): Use as 10 mg/ml concentration. A starting dose of 5 mg is recommended, repeated at 4-hourly intervals in opioid-naïve patients 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 naïve patients, titrating gradually according to symptom control. Cancer patients transferring from oral oxycodone may require much higher doses (see below).

Particular attention should be paid to the treatment of opiode side effects.

Conversion from morphine
The dose should be based on the following ratio: 1 mg of parenteral morphine 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 the dosage is carefully titrated to each individual patient. Initially, a lower-than equivalent dose may be advisable.

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, if only a few doses have been given. In case of shift in choice of opioid to a patient, who has been in long-term opioid-treatment (opioidrotation), it should be emphasised that the above mentioned equipotent doses are guidance only. Often it is necessary to administer less a decreased dose as equipotency recommend. Based on this and the patients interindividual variability a shift requires that the dosing is titrated carefully for every single patient.

This medicinal product is for single use only, any unused solution should be discarded.

Lindoxa 10 mg/ml solution for injection/infusion and Lindoxa 20 mg/2 ml solution for injection/infusion may be diluted with
- Water for injections
- Sodium chloride 9 mg/mL (0.9%) solution for injection
- Glucose 50 mg/mL (5%) solution for injection
- Ringer's solution for injection
- Sodium chloride and Glucose solution for injection
  (Sodium chloride 0.18% w/v and Glucose 4% w/v)
- Lactated Ringer's solution for injection
  (Ringer Lactate solution and 5% Glucose solution).

Oxycodone hydrochloride, that was used undiluted or diluted to 1 mg/ml in various studies with different infusion solutions and under the use of representative brands of polypropylene or polycarbonate syringes, polyethylene or PVC tubing and PVC or EVA infusion bags, does not have to be protected against light.

Shelf-life 5 years.

After dilution:
Chemical and physical in-use stability has been demonstrated for 48 hours/days 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 are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8 °C, unless reconstitution, dilution has taken place in controlled and validated aseptic conditions.