

NA. NOLXADO prolonged - release tablets 16 pivo stran

Package leaflet: Information for the patient

Nolxado 10 mg/5 mg  
prolonged-release tablets  
Nolxado 20 mg/10 mg  
prolonged-release tablets  
Nolxado 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

- What Nolxado is and what it is used for
- What you need to know before you take Nolxado
- How to take Nolxado
- Possible side effects
- How to store Nolxado
- Contents of the pack and other information

1. What Nolxado is and what it is used for

Pain relief

You have been prescribed **Nolxado** for the treatment of severe pain, which can be adequately managed only with opioid analgesics.

How Nolxado work in pain relief

**Nolxado** contains oxycodone hydrochloride and naloxone hydrochloride as active substances. Oxycodone is responsible for the painkilling effect of **Nolxado**. It is a strong analgesic ('painkiller') that belongs to a group of medicines called opioids. Naloxone is intended to bring relief from some side effects of treatment with strong painkillers.

2. What you need to know before you take Nolxado

Do not take Nolxado:

- if you are allergic to oxycodone or naloxone or any of the other ingredients of this medicine (listed in section 6)
- if you have breathing problems, such as breathing more slowly or weakly than expected (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 a type of bowel obstruction (paralytic ileus) not caused by opioids;
- if you have moderate to severe liver problems.

Warnings and precautions

Talk to your doctor or pharmacist before taking Nolxado:

- in the case of elderly or debilitated (weak) patients;
- if you have a type of bowel obstruction (paralytic ileus) caused by opioids;
- if you have kidney problems;
- if you have mild liver problems;
- if you have severe lung problems (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 disorder as a result of an intoxication (toxic psychosis);
- if you suffer from gallstone problems;
- if your prostate gland is abnormally enlarged (prostate hypertrophy);
- if you are or ever have been addicted to alcohol or drugs, or have previously suffered from withdrawal symptoms such as agitation, anxiety, shaking or sweating upon stopping alcohol or drugs;
- if your pancreas is inflamed (pancreatitis);
- if you have low blood pressure (hypotension);
- if you have high blood pressure (hypertension);
- if you have heart problems;
- if you have a head injury (due to the risk of increased brain pressure);
- if you suffer from epilepsy or are prone to fits;
- if you are also taking a type of medicine known as a MAO inhibitor (used to treat depression or Parkinson's disease) e.g. medicines containing tranlycypromine, phenelzine, isocarboxazid, moclobemide and linezolid;
- if sleepiness or episodes of suddenly falling asleep occur.

Nolxado is not recommended for use in patients with advanced digestive or pelvic cancers where bowel obstruction may be a problem.

How to use Nolxado correctly

If you experience severe diarrhoea at the start of treatment (within the first 3-5 days) this may be due to the effect of naloxone. It may be a sign that your bowel movements are returning to normal. If diarrhoea persists after 3-5 days, or it gives you cause for concern, please contact your doctor.

If you have been using high doses of another opioid, withdrawal symptoms (such as restlessness, bouts of sweating or muscle pain) may occur when you initially switch to Nolxado. If you experience withdrawal symptoms, you may need to be specially monitored by your doctor.

If you need to undergo surgery, please tell your doctor that you are taking Nolxado.

If you have been taking Nolxado for a long time, you may become tolerant. This means you may need a higher dose to achieve the desired effect. Long-term use of Nolxado may also lead to addiction. Withdrawal symptoms may occur if treatment is stopped too suddenly. If you no longer need treatment, you should reduce your daily dose gradually, in consultation with your doctor.

As with other strong opioid painkillers, there is a risk that you may develop a psychological dependence to oxycodone.

You may notice remains of the tablet in your stools. Do not be alarmed, as the active substances will have already been released in the stomach and gut, and absorbed into your body.

Incorrect use of Nolxado

Nolxado is not suitable for withdrawal treatment.

Nolxado should never be abused, particularly if you have a drug addiction. If you are addicted to drugs such as heroin, morphine or methadone, severe withdrawal symptoms are likely if you abuse Nolxado because they contain the active substance naloxone. Pre-existing withdrawal symptoms may be made worse.

You should never misuse Nolxado by dissolving and injecting them (e.g. into a blood vessel). They contain talc, which can cause destruction of local tissue (necrosis) and changes in lung tissue (lung granuloma). Misuse can also have other serious consequences which may be fatal.

The use of Nolxado may produce positive results in drugs tests.

The use of Nolxado as a doping agent may become a health hazard.

Children and adolescents

Nolxado must not be given to children or adolescents under 18 years of age as the safety and benefits have not been shown yet.

Other medicines and Nolxado

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 Nolxado at the same time as medicines which affect the way the brain works. For example, you may feel very sleepy, or breathing problems may get worse.

Examples of medicines that affect the way the brain works include:

- other strong painkillers (opioids);
- sleep medicines and tranquillisers (sedatives, hypnotics);
- antidepressants;
- medicines used to treat allergies, travel sickness or nausea (antihistamines or antiemetics);
- other medicines which act on the nervous system (phenothiazines, neuroleptics).

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);
- antifungal medicines of the –azole type (e.g. ketoconazole);
- ritonavir or other protease inhibitors (used to treat HIV);
- 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).

Nolxado with drink and alcohol

Drinking alcohol whilst taking Nolxado 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 Nolxado. You should avoid drinking grapefruit juice while you are taking Nolxado.

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

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

Breastfeeding

Breastfeeding should be discontinued during treatment with Nolxado.

Oxycodone passes into breast milk. It is not known whether naloxone also passes into breast milk. Therefore, a risk for the suckling infant cannot be excluded, in particular following intake of multiple doses of Nolxado.

Driving and using machines

This medicine may affect your ability to drive or operate machines. This is most likely at the start of your treatment, after a dose increase or after switching from a different medication. These side effects should disappear once you are on a stable dose.

This medicine 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.

Ask your doctor whether you may drive or operate machines.

Nolxado contains lactose.

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

3. How to take Nolxado

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

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 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 depending on 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, your treatment with Nolxado may 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 without naloxone. However, the maximum daily dose of oxycodone should not exceed 400 mg. The beneficial effect of naloxone on bowel movements may be affected if additional oxycodone is given without additional naloxone.

If you experience pain between doses, you may need to take an additional fast-acting painkiller. Nolxado is not suitable for this. Please talk to your doctor.

If you feel that Nolxado is too strong or too weak, please talk to your doctor or pharmacist.

Elderly patients

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

Hepatic or renal impairment

If you have kidney or mild liver problems your doctor may prescribe a lower dose. You must not take Nolxado if you have moderate or severe liver problems, (see also Section 2 'Do not take **Nolxado**' and 'Warnings and Precautions').

Use in children and adolescents

No studies have been carried out to show that Nolxado works properly in children and adolescents, or are safe for them to take. They are therefore not recommended for use in patients under 18 years of age.

Method of administration

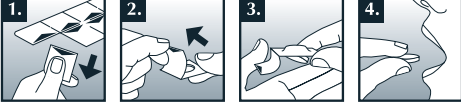
Oral use.

Swallow Nolxado whole with a glass of water. You can take Nolxado with or without food. Take them every 12 hours. For instance, if you take a tablet at 8 o'clock in the morning, you should take your next tablet at 8 o'clock in the evening. Do not divide, break, chew or crush the tablets.

**Taking divided, broken, chewed or crushed tablets may result in your body absorbing a potentially fatal dose of oxycodone (see under 'If you take more Nolxado than you should').**

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

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



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

Duration of use

You should not take Nolxado for any longer than you need to. If you have been taking Nolxado for a long time your doctor should regularly check that you still need them.

If you take more Nolxado than you should

If you have taken more than the prescribed dose, you must inform your doctor immediately.

An overdose may result in:

- a reduction in size of pupils in the eye;
- breathing more slowly or weakly than expected (respiratory depression);
- drowsiness or loss of consciousness;
- low muscle tone (hypotonia);
- reduced pulse rate;
- a fall in blood pressure.

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

You should avoid situations which require you to be alert, e.g. driving.

If you forget to take Nolxado,

or if you take a lower dose than the one prescribed, you may not feel any effect.

- If you forget to take your dose and your next usual dose is due in 8 hours or more: Take the forgotten dose immediately and continue with your normal dosing routine.
- If your next usual dose is due in less than 8 hours: Take the forgotten dose, then, wait another 8 hours before taking your next dose. Try to get back in your normal dosing routine (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 Nolxado

Do not stop taking Nolxado without first speaking with your doctor. If you do not require any further treatment, your doctor will advise you how to reduce the daily dose gradually. 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 or signs to look out for, and what to do if you are affected:**

The most serious side effect is a condition where you breathe more slowly or weakly than expected (respiratory depression). It mostly occurs in elderly and weak patients. Opioids can also cause a severe drop in blood pressure in susceptible patients. If you are affected by these important side effects, consult a doctor immediately.

The following side effects have been seen in patients being treated for pain

**Common** (may affect up to 1 in 10 people)

- abdominal pain
- constipation
- diarrhoea
- dry mouth
- indigestion
- vomit (be sick)
- feel sick
- wind
- decreased appetite up to loss of appetite

- a feeling of dizziness or 'spinning'
- headache
- hot flushes
- general 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
- palpitations
- biliary colic
- chest pain
- generally feeling unwell
- pain
- swelling of the hands, ankles or feet
- difficulties to concentrate
- impaired speaking
- shaking
- difficulties breathing
- restlessness
- chills
- hepatic enzymes increased
- rise in blood pressure
- 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
- dental changes
- weight gain
- yawning

**Not known** (frequency cannot be estimated from available data)

- euphoric mood
- severe drowsiness
- erectile dysfunction
- nightmares
- hallucinations
- shallow breathing
- difficulty in passing urine
- tingling in hands or feet
- belching

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

Breathing problems, such as breathing more slowly or weakly than expected (respiratory depression), reduction in size of the pupils in the eye, muscle cramps and decreased 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
- taste anomalies
- increased muscle tension
- involuntary muscle contractions
- drug dependence
- ileus
- dry skin

- PMS-433U-KRKA

Šifra: xxxxxx
Emb. mat.: NA. NOLXADO TPOS IE
Dimenzije: 289 ± 0,5 mm x 6,55 ± 0,8 mm
Materijal: papir tip C
PhC št.: xxx
Merilo: 1:1
Datum: 06.04.2017
Izdelač: A. Mohorič
Pregledal: K. Peric
Oddelek za oblikovanje





- 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)
- reduced sexual drive
- flushing of skin
- dehydration
- agitation
- thirst

- Rare** (may affect up to 1 in 1,000 people)
- itching rash (urticaria)
  - herpes simplex
  - increased appetite
  - black (tarry) stools
  - gingival bleeding

- Not known** (frequency cannot be estimated from the available data)
- acute generalized allergic reactions (anaphylactic reactions)
  - absence of menstrual periods
  - problems with bile flow

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 via 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 Nolxado

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 30°C.

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 Nolxado contains

- The active substances are oxycodone hydrochloride and naloxone hydrochloride.

10 mg/5 mg prolonged-release tablets:

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.

20 mg/10 mg prolonged-release tablets:

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.

40 mg/20 mg prolonged-release tablets:

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:

10 mg/5 mg prolonged-release tablets:

hydroxypropylcellulose, ethylcellulose, glyceryol 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 "Nolxado contains lactose".

20 mg/10 mg prolonged-release tablets:

hydroxypropylcellulose, ethylcellulose, glyceryol 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 "Nolxado contains lactose".

40 mg/20 mg prolonged-release tablets:

hydroxypropylcellulose, ethylcellulose, glyceryol 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 "Nolxado contains lactose".

What Nolxado looks like and contents of the pack

10 mg/5 mg prolonged-release tablets:

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).

20 mg/10 mg prolonged-release tablets:

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).

40 mg/20 mg prolonged-release tablets:

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).

Nolxado 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.

Nolxado 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. Nolxado 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.

Only for perforated unit dose child-resistant peel-off blisters:

Nolxado 10 mg/5 mg is available in packs containing 10x1, 14x1, 20x1, 28x1, 30x1, 50x1, 56x1, 60x1, 90x1, 98x1, 100x1 or 112x1 prolonged-release tablets in perforated unit dose child-resistant peel-off blisters.

Nolxado 20 mg/10 mg is available in packs containing 10x1, 20x1, 28x1, 30x1, 50x1, 56x1, 60x1, 90x1, 98x1, 100x1 or 112x1 prolonged-release tablets in perforated unit dose child-resistant peel-off blisters.

Nolxado 40 mg/20 mg is available in packs containing 10x1, 20x1, 28x1, 30x1, 50x1, 56x1, 60x1, 90x1, 98x1, 100x1 or 112x1 prolonged-release tablets in perforated unit dose child-resistant peel-off blisters.

Not all pack sizes may be marketed.

Marketing Authorisation Holder

HCS bvba, H. Kennisstraat 53, B 2650 Edegem, Belgium

Manufacturer

KRKA, d.d., Novo mesto, Šmarješka cesta 6, 8501 Novo mesto, Slovenia

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

Germany	Oxycodon/Naloxon Krka
Belgium	Oxycodon/Naloxon HCS
Bulgaria	Адонакс
Czech Republic, Estonia	Noldoxen
Denmark	Oxycodone/Naloxone Krka
Spain, Ireland	Nolxado
Finland, Sweden	Oxycodone/Naloxone Krka
Croatia, Hungary, Slovenia, Slovakia	Adolax
Lithuania, Romania	Dolnada
Latvia, Poland	Oxynador
Portugal	Oxicodona + Naloxona HCS
United Kingdom	Oxycodone hydrochloride/ Naloxone hydrochloride HCS bvba

This leaflet was last revised in