Package leaflet: Information for the user

<Invented name> 2.5 mg/1.25 mg prolonged-release tablets
<Invented name> 15 mg/7.5 mg prolonged-release tablets
<Invented name> 30 mg/15 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:

1. What <Invented name> is and what it is used for

<Invented name> contains oxycodone hydrochloride and naloxone hydrochloride as active substances.

<Invented name> is only for use in adults.

<Invented name> is used for the treatment of severe pain, which can be adequately managed only with opioid analgesics.

How <Invented name> works
Oxycodone hydrochloride is responsible for the pain-killing effect of <Invented name>, and is a potent analgesic ("painkiller") of the opioid group. The second active substance of <Invented name>, 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 <Invented name>

Do not take <Invented name>:
- 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 to 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.

Warnings and precautions

Talk to your doctor or pharmacist before taking <Invented name>**:**
- 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 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,
- 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), e.g. medicines containing tranylcypromine, phenelzine, isocarboxazid, moclobemide and linezolid.

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 <Invented name>.

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.

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 <Invented name> 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 <Invented name> 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.

If taken over the long term, you may become tolerant to <Invented name>. This means you may need a higher dose to achieve the desired effect. Also, long-term use may lead to physical dependence. Withdrawal symptoms may occur if treatment is stopped too suddenly (restlessness, bouts of sweating, muscle pain). If you no longer need treatment, you should reduce your daily dose gradually, in consultation with your doctor.

The active substance oxycodone hydrochloride alone has an abuse profile similar to other strong opioids (strong analgesics). There is potential for development of psychological dependence. Oxycodone hydrochloride containing products should be avoided in patients with a present or past abuse of alcohol, drugs or medicines.
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 <Invented name>.

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 <Invented name>

<Invented name> isnot suitable for withdrawal treatment.

<Invented name> 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 <Invented name> because it contains the ingredient naloxone. Pre-existing withdrawal symptoms may be made worse.

You should never misuse the prolonged-release 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 <Invented name> may produce positive results in doping controls.

The use of <Invented name> as a doping agent may become a health hazard.

Other medicines and <Invented name>

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

If you take <Invented name> at the same time as you take other medicines, the effect of <Invented name> or the other medicine may be changed.
Tell your doctor if you are taking:

- other potent painkillers (opioids);
- sleep medication and tranquilisers (sedatives, hypnotics);
- medicines to treat depression;
- medicines used to treat allergies, travel sickness or nausea (antihistamines or antiemetics);
- medicines to treat psychiatric or mental disorders (phenothiazines, neuroleptics, antipsychotics);
    - 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, itraconizole or posaconizole);
    - a specific type of medicine known as aprotease 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 <Invented name> and paracetamol, acetylsalicylic acid or naltrexone.

<Invented name> with food, drink and alcohol

Drinking alcohol whilst taking <Invented name> 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 <Invented name>.

You should avoid drinking grapefruit juice while you are taking <Invented name>.

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 <Invented name> 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 <Invented name>. 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 <Invented name>.

Driving and using machines

<Invented name> may affect your ability to drive or operate machines. In particular, this is likely at the start of therapy, after a dose increase or after switching from a different medicine. However, these side effects disappear once you are on a stable dose.

Ask your doctor whether you may drive or operate machines.

<Invented name> 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 this medicine.

3. How to take <Invented name>

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

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

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 dose 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, <Invented name> 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 <Invented name> to another opioid pain medication your bowel function will probably worsen.

If you experience pain between two doses of <Invented name>, you may need a rapid-acting painkiller. <Invented name> is not suitable for this. In this case, please talk to your doctor.

If you have the impression that the effect of <Invented name>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.

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 <Invented name> with special caution. If you have a moderate or severe impairment of liver function, <Invented name> should not be used (see also Section 2 “Do not take <Invented name>” and “Warnings and precautions”).

Children and adolescents below 18 years of age
<Invented name> 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, <Invented name> use in children and adolescents under 18 years of age is not recommended.

Method of administration

<Invented name> is for oral use.

Swallow the prolonged-release tablets whole, with sufficient liquid (½ glass of water). You can take the prolonged-release tablets with or without food. Take these tablets every 12 hours, according to a fixed time schedule.

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 <Invented name> than you should”).

Duration of use
In general, you should not take <Invented name> for any longer than you need to. If you are on long-term treatment , your doctor should regularly check whether you still need <Invented name>.

If you take more <Invented name> than you should
If you have taken more than the prescribed dose , 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, and
- a drop in blood pressure.

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 <Invented name>

Or if you take a dose lower than the one prescribed, you may not feel any painkilling 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 <Invented name>

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 or signs 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.

Common (may affect 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
- palpitations
- runny nose

- 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
- 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
- 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
- yawning
- weight gain

Not known

- euphoric mood
- severe drowsiness
- erectile dysfunction
- nightmares
- hallucinations
- shallow breathing
- difficulties in passing urine
- tingling skin (pins and needles)
- belching

<u>The active substance oxycodone hydrochloride, if not combined with naloxone hydrochloride, is known to have following, differing side-effects:</u>

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 depressing 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
- drug dependence
- 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
- difficulties 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 females

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

- itching rash (urticaria)
- infections such as cold sores
- increased appetite
- black (tarry) stools
- bleeding gums

or herpes (which may cause blisters around the mouth or genital area)

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
- aggression
- problems with bile flow
- tooth decay

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 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 <Invented name>

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 carton and blister, after "EXP…". The expiry date refers to the last day of that month.

Do not store above 25°C.

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 to protect the environment.

6. Contents of the pack and other information

What <Invented name> contains

The active substances are: oxycodone hydrochloride and naloxone hydrochloride.

<Invented name> 2.5 mg/1.25 mg
Each prolonged-release tablet contains 2.5 mg oxycodone hydrochloride, equivalent to 2.25 mg oxycodone and 1.25 mg naloxone hydrochloride as
1.37 mg naloxone hydrochloride dihydrate, equivalent to 1.13 mg naloxone.

<Invented name> 15 mg/7.5 mg
Each prolonged-release tablet contains 15 mg oxycodone hydrochloride, equivalent to 13.5 mg oxycodone and 7.5 mg naloxone hydrochloride as8.24 mg naloxone hydrochloride dihydrate, equivalent to 6.75 mg naloxone.

<Invented name> 30 mg/15 mg
Each prolonged-release tablet contains 30 mg oxycodone hydrochloride, equivalent to 27 mg oxycodone and 15 mg naloxone hydrochloride as 16.48 mg naloxone hydrochloride dihydrate, equivalent to 13.5 mg naloxone.

The other ingredients are:

<Invented name> 2.5 mg/1.25 mg
Tablet core:
Hydroxypropylcellulose, ethylcellulose, stearyl alcohol, lactose monohydrate, talc, magnesium stearate
Tablet coat:
Polyvinyl alcohol, partially hydrolysed, titanium dioxide (E171), macrogol 3350, talc, iron oxide red (E172), iron oxide yellow (E172)

<Invented name> 15 mg/7.5 mg
Tablet core:
Hydroxypropylcellulose, ethylcellulose, stearyl alcohol, lactose monohydrate, talc, magnesium stearate
Tablet coat:
Polyvinyl alcohol, partially hydrolysed, titanium dioxide (E171), macrogol 3350, talc, iron oxide black (E172), iron oxide red (E172), iron oxide yellow (E172)

<Invented name> 30 mg/15 mg
Tablet core:
Povidone K30, ethylcellulose, stearyl alcohol, lactose monohydrate, talc, magnesium stearate
Tablet coat:
Polyvinyl alcohol, partially hydrolysed, titanium dioxide (E171), macrogol 3350, talc, iron oxide black (E172), iron oxide red (E172), iron oxide yellow (E172)

What <Invented name> looks like and contents of the pack

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

<Invented name> 2.5 mg/1.25 mg
Light yellow, round tablets, 5 mm in diameter, with a film coating.

<Invented name> 15 mg/7.5 mg
Grey, capsule shaped tablets, with a nominal length of 9.5 mm and with a film coating, embossed "OXN" on one side and "15" on the other.

<Invented name> 30 mg/15 mg
Brown, capsule shaped tablets, with a nominal length of 9.5 mm and with a film coating, embossed "OXN" on one side and "30" on the other.

<Invented name> is available in blister packs of 10, 14, 20, 28, 30, 50, 56, 60, 98 and 100 prolonged-release tablets.

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:

Austria	Armoneve 2.5 mg/1.25 mg <15 mg/7.5 mg> <30 mg/15 mg> Retardtabletten
Belgium	Oxsynia 2,5 mg/1,25 mg <15 mg/7,5 mg> <30 mg/15 mg> tabletten met verlengde afgifte
Bulgaria	Armoneve 2.5 mg/1.25 mg <15 mg/7.5 mg> <30 mg/15 mg> Таблетка с удължено освобождаване
Czech Republic	Armoneve
Germany	Oxycodon / Naloxon Krugmann 2,5 mg/1,25 mg Retardtabletten Oxycodon / Naloxon Krugmann 15 mg/7,5 mg Retardtabletten Oxycodon / Naloxon Krugmann 30 mg/15 mg Retardtabletten
Denmark	Armoneve
Estonia	Oxsynia
Finland	Armoneve
France	OXSYNIA LP 2,5 mg/1,25 mg <15 mg/7,5 mg> <30 mg/15 mg> Comprimé à libération prolongée
Hungary	Armoneve
Ireland	Armoneve 2.5 mg/1.25 mg <15 mg/7.5 mg> <30 mg/15 mg> prolonged-release tablets

Italy	Oxsynia
Latvia	Armoneve 2.5 mg/1.25 mg <15 mg/7.5 mg> <30 mg/15 mg> Ilgstošās darbības tablete
Luxembourg	Oxsynia - 2,5 mg/1,25 mg <15 mg/7,5 mg> <30 mg/15 mg>
The Netherlands	Armoneve 2.5 mg/1.25 mg <15 mg/7.5 mg> <30 mg/15 mg>, tabletten met verlengde afgifte
Poland	Armoneve
Portugal	Armoneve
Romania	Oxsynia 2.5 mg/1.25 mg <15 mg/7.5 mg> <30 mg/15 mg> Comprimate cu eliberare prelungită
Slovakia	Armoneve 2.5 mg/1.25 mg <15 mg/7.5 mg> <30 mg/15 mg> Tableta s pred´lženým uvoľňovaním
Slovenia	Armoneve 2.5 mg/1.25 mg tablete s podaljšanim sproščanjem Armoneve 15 mg/7.5 mg tablete s podaljšanim sproščanjem Armoneve 30 mg/15 mg tablete s podaljšanim sproščanjem
Sweden	Armoneve
United Kingdom	Armoneve 2.5 mg/1.25 mg <15 mg/7.5 mg> <30 mg/15 mg> prolonged-release tablets

This leaflet was last revised in {MM/YYYY}.
[To be completed nationally]