Package leaflet: Information for the user

Targinact® 10 mg/5 mg prolonged-release tablets
(oxycodone hydrochloride and 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.

The name of your medicine is Targinact® 10 mg/5 mg prolonged-release tablets but will be referred to as Targinact or Targinact tablets throughout this leaflet. Please note that this leaflet also contains information about the other strengths such as Targinact 5 mg/2.5 mg, 20 mg/10 mg and 40 mg/20 mg prolonged-release tablets.

What is in this leaflet:

1. What Targinact tablets are and what they are used for

Targinact 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 Targinact tablets for the treatment of severe pain, which can be adequately managed only with opioid analgesics. Naloxone is added to counteract constipation.

How these tablets work in pain relief
These tablets contain oxycodone hydrochloride and naloxone hydrochloride as active substances.
Oxycodone is responsible for the painkilling effect of the tablets. It is a strong analgesic ('painkiller') that belongs to a group of medicines called opioids. Naloxone is intended to bring relief from constipation. Constipation is a typical side effect of treatment with strong painkillers.

Restless legs syndrome
You have been prescribed Targinact tablets for the second line symptomatic treatment of severe to very severe restless legs syndrome in people who can't be treated with dopamine medicines. People with restless legs syndrome have unpleasant sensations in their limbs. This can start as soon as they sit or lie down and is only relieved by an irresistible urge to move the legs, sometimes the arms and other parts of the body. It makes sitting still and sleeping very difficult. Naloxone hydrochloride is added to counteract constipation.

How these tablets work in restless legs syndrome
These tablets help to relieve the unpleasant sensations and so reduces the urge to move the limbs. Naloxone is intended to bring relief from constipation. Constipation is a typical side effect of treatment with strong painkillers.

2. What you need to know before you take Targinact tablets

Do not take Targinact tablets
- if you are allergic (hypersensitive) to oxycodone or naloxone, or any of the other ingredients of the tablets (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.

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

Warnings and Precautions
Talk to your doctor or pharmacist before taking these tablets:
- 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 tranylcypromine, phenelzine, isocarboxazid, moclobemide and linezolid;
- if sleepiness or episodes of suddenly falling asleep occur.

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 them 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.

You must swallow the tablet whole, so as not to affect the slow release of oxycodone hydrochloride from the 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 Targinact than you should").

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 another opioid, withdrawal symptoms (such as restlessness, bouts of sweating or muscle pain) may occur when you initially switch to taking these tablets. If you experience withdrawal symptoms, you may need to be specially monitored by your doctor.

If you have been taking these tablets 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 these tablets 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.

Tell your doctor if you have advanced digestive or pelvic cancers where bowel obstruction may be a problem.

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

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

Incorrect use of Targinact tablets
These tablets are not suitable for withdrawal treatment. These tablets 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 these tablets because they contain the ingredient naloxone. Pre-existing withdrawal symptoms may be made worse.

You should never misuse the tablets 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 these tablets may produce positive results in drugs tests.

Other medicines and Targinact tablets
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. If you take these tablets at the same time as you take other medicines, the effect of these tablets or the other medicine may be changed. Tell your doctor if you are taking:
- other strong painkillers (opioids);
- sleep medication and tranquillisers (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, 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).
- 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).

Targinact tablets with food, drink and alcohol
Drinking alcohol whilst taking Targinact 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 Targinact.
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 during pregnancy should be avoided unless your doctor thinks treatment with this medicine is essential. If used over prolonged periods during pregnancy, oxycodone may lead to withdrawal symptoms in the newborn baby. If oxycodone is given during childbirth, the baby may have breathing problems (respiratory depression).

Breastfeeding
Breastfeeding should be stopped during treatment with these tablets as oxycodone (one of the active ingredients of your medicine) passes into breast milk.

Driving and using machines
This medicine can affect your ability to drive as it may make you sleepy or dizzy. 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.
- Do not drive while taking this medicine until you know how it affects you.
- It is an offence to drive while you have this medicine in your body over a specified limit unless you have a defence (called the 'statutory defence').
- This defence applies when:
  - 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 and in the information provided with the medicine.
- Please note that it is still an offence to drive if you are unfit because of the medicine (i.e. your ability to drive is being affected).

Details regarding a new driving offence concerning driving after drugs have been taken in the UK may be found here: https://www.gov.uk/drug-driving-law.

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

Targinact tablets contain lactose
These tablets contain lactose (milk sugar). If you have been told that you have an intolerance to some sugars, contact your doctor before taking these tablets.

3. How to take Targinact tablets

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

Targinact 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 these prolonged-release tablets whole so as not to affect the slow release of oxycodone from the tablets. Do not break, chew or crush these tablets. Taking broken, chewed or crushed tablets may result in your body absorbing a potentially fatal dose of oxycodone (see section 3: 'If you take more Targinact tablets 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 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 these tablets 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 are switched from these tablets to another opioid pain medication your bowel function will probably worsen.

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

If you feel that these tablets are too strong or too weak, please talk to your doctor or pharmacist.

To treat restless legs syndrome

Adults
The usual starting dose is 5 mg oxycodone hydrochloride/ 2.5 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. They will also decide on any necessary dose adjustments during treatment. Your dose will be adjusted according to your individual sensitivity. You should be given the lowest dose needed to relieve your restless legs syndrome symptoms.
If you feel that these tablets are 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.

To treat pain or restless legs syndrome

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

Liver or kidney problems
If you have kidney or mild liver problems your doctor may prescribe a lower dose. You must not take these tablets if you have moderate or severe liver problems,
(see also Section 2 'Do not take Targinact tablets' and 'Take special care with Targinact tablets' and 'Warnings and Precautions').

Children and adolescents below 18 years of age
No studies have been carried out to show that these tablets work 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
Swallow your tablets whole with a glass of water. You can take these tablets 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 break, chew or crush the tablets (see section 2 'Warnings and precautions').

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

If you take more Targinact tablets 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 up to 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 Targinact tablets,
or if you take a lower dose than the one prescribed, you may not feel any effect.

If you should 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 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 Targinact tablets
Do not stop taking these tablets 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 these tablets, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, these tablets 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 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 the 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
- 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 skin (pins and needles)
- belching

The active ingredient 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
- 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
- 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 females

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
- aggression
- problems with bile flow
- 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'
- difficulty in concentrating
- 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)
- 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
- 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, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.
By reporting of side effects, you can help provide more information on the safety of this medicine.

5. How to store Targinact tablets

Keep all medicines out of the sight and reach of children.

Do not use any tablets after the expiry date which is stated on the carton and blister, after 'Exp...'. The expiry date refers to the last day of the month.

Do not store above 25°C. Store in the original package in order to protect from light.

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.

If your tablets become discoloured or show any signs of deterioration, seek the advice of your pharmacist.

6. Contents of the pack and other information

What Targinact contains
The active ingredients in Targinact are oxycodone hydrochloride and naloxone hydrochloride.

Each 10 mg/5 mg tablet contains 10 mg of oxycodone hydrochloride (equivalent to 9 mg oxycodone), and 5.45 mg naloxone hydrochloride dihydrate (equivalent to 5 mg naloxone hydrochloride and 4.5 mg naloxone).

The other ingredients are:

Tablet core: povidone K30, ethyl cellulose, stearyl alcohol, lactose monohydrate, talc, magnesium stearate.

Tablet coat: polyvinyl alcohol, titanium dioxide (E171), macrogol 3350, talc.

What Targinact looks like and contents of the pack
Targinact 10 mg/5 mg tablets are white, oblong, film coated tablets, marked 'OXN' on one side and '10' on the other.

Targinact tablets are available in pack sizes of 28 tablets.

Who makes and repackages your medicine?
Your medicine is manufactured by Mundipharma GmbH, Mundipharma str.2, 65549 Limburg, Germany or
Bard Pharmaceuticals Limited, 191 Cambridge Science Park, Milton Road, Cambridge CB4 0GW, UK. Procured from within the EU and repackaged by Product Licence Holder: Primecrown Ltd., 4/5 Northolt Trading Estate, Belvue Road, Northolt, Middlesex, UB5 5QS.

PL 10383/1997 Targinact 10 mg/5 mg prolonged-release tablets

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Leaflet date: 02.11.2017

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