Package leaflet: Information for the patient

Mysimba 8 mg/90 mg prolonged-release tablets
naltrexone hydrochloride/bupropion hydrochloride

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

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 Mysimba is and what it is used for

Mysimba contains 2 active substances: naltrexone hydrochloride and bupropion hydrochloride and is used in obese or overweight adults to manage weight together with a reduced calorie diet and physical exercise. This medicine works on areas on the brain involved in the control of food intake and energy expenditure.

Obesity in adults over 18 years of age is defined as a body mass index of greater than or equal to 30 and overweight in adults over 18 years of age is defined as a body mass index greater than or equal to 27 and less than 30. The body mass index is calculated as the measured body weight (kg) divided by the measured height squared (m^2).

Mysimba is approved for use in patients with an initial body mass index of 30 or greater; it can also be given to those with a body mass index between 27 and 30 if they have additional weight-related conditions such as controlled high blood pressure (hypertension), type 2 diabetes or high levels of lipid (fat) in the blood.

Mysimba may be discontinued by your doctor after 16 weeks if you have not lost at least 5 percent of your initial body weight. Your doctor may also recommend stopping treatment if there are concerns about increased blood pressure, or other concerns with the safety or tolerability of this medicine.

2. What you need to know before you take Mysimba

Do not take Mysimba:
- if you are allergic to naltrexone, to bupropion or to any of the other ingredients of this medicine (listed in section 6);
- if you have an abnormally high blood pressure (hypertension) that is not controlled using a medicinal product;

- if you have a condition that causes fits (seizures) or if you have a history of fits;
- if you have a brain tumour;
- if you are usually a heavy drinker and you have just stopped drinking alcohol, or are going to stop while you are taking Mysimba;
- if you have recently stopped taking sedatives or medicines to treat anxiety (especially benzodiazepines), or if you are going to stop them while you are taking Mysimba;
- if you have or have had a bipolar disorder (extreme mood swings);
- if you are using any other medicines which contain bupropion or naltrexone;
- if you have an eating disorder or had one in the past (for example, bulimia or anorexia nervosa);
- if you are currently dependent on chronic opiates or opiate agonists (for example methadone), or you are going through acute withdrawal (cold turkey);
- if you are taking medicines for depression or Parkinson's disease called monoamine oxidase inhibitors (MAOIs) or have taken them in the last 14 days;
- if you have severe liver disease;
- if you have endstage kidney disease.

Warnings and precautions
Talk to your doctor or pharmacist before taking Mysimba.
This is important because some conditions make it more likely that you could have side effects (see also section 4).

If you feel **depressed, contemplate suicide, have a history of attempting suicide or any other mental health problems,** you should inform your doctor before taking this medicine.

Fits (seizures)
Mysimba has been shown to cause fits (seizures) in up to 1 in 1,000 patients (see also section 4). You should inform your doctor before taking this medicine:
- if you have had a serious head injury or head trauma;
- if you regularly drink alcohol (see "Mysimba with alcohol");
- if you regularly use medicines to help you to sleep (sedatives);
- if you are currently dependent on or addicted to cocaine or other stimulating products;
- if you have diabetes for which you use insulin or oral medicines that may cause low sugar levels in your blood (hypoglycaemia); or
- if you are taking medicines that may increase the risk of fits (see "Other medicines and Mysimba").

If you have a fit (seizure), you should stop taking Mysimba and consult your doctor immediately.

You should stop taking Mysimba immediately and consult your doctor if you are experiencing any symptoms of an **allergic reaction** such as swelling of the throat, tongue, lips, or face, difficulty swallowing or breathing, dizziness, fever, rash, pain in the joints or in the muscles, itching or hives after taking this medicine (see also section 4).

You should talk to your doctor, especially if:
- you have **high blood pressure** before taking Mysimba, because it can become worse. You will have your blood pressure and heart rate measured before you start taking Mysimba and while you are taking it. If your blood pressure or heart rate increases significantly, you may need to stop taking Mysimba.
- you have uncontrolled **coronary artery disease** (a heart disease caused by poor blood flow in the blood vessels of the heart) with symptoms such as angina (characterised by chest pain) or a recent heart attack.
- you already have or have had a condition affecting the circulation of blood in the brain (**cerebrovascular disease**).
- you have any **liver problems** before you start Mysimba.
- you have any **kidney problems** before you start Mysimba.
- you have a history of **mania** (feeling elated or over-excited, which causes unusual behaviour).

Older People
Use caution when taking Mysimba, if you are 65 years or older. Mysimba is not recommended if you are over 75 years.

Children and adolescents
No studies have been conducted in children and adolescents under the age of 18. Therefore Mysimba should not be used in children and adolescents below 18 years.

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

Do not take Mysimba with:
- **Monoamine oxidase inhibitors** (medicines to treat depression or Parkinson's disease) such as phenelzine, selegiline, or rasagiline. You must stop taking these medicines for at least 14 days before starting Mysimba (see "Do not take Mysimba").
- **Opiates and opiate-containing medicines** for example to treat cough and cold (such as mixtures containing dextromethorphan or codeine), opiate addiction (such as methadone), pain (for example, morphine and codeine), diarrhoea (for example, paregoric). You must have stopped taking any opiate medicines at least 7-10 days before starting Mysimba. Your doctor may carry out a blood test to ensure that your body has cleared these medicines before starting your treatment. Naltrexone blocks the effects of opiates; if you take higher doses of opiates to overcome these effects of naltrexone, you may suffer from an acute opiate intoxication which may be life threatening. After you stop treatment with Mysimba you may be more sensitive to low doses of opiates (see "Do not take Mysimba").

Tell your doctor if you are taking any of the following medicines, as your doctor will closely monitor you for side effects:
- Medicines that may, when used alone or in combination with naltrexone/bupropion, increase the **risk of fits** such as:
  - medicines for depression and other mental health problems;
  - steroids (except drops, creams, or lotions for eye and skin conditions or inhalers for breathing disorders such as asthma);
  - medicines used to prevent malaria;
  - quinolones (antibiotics such as ciprofloxacine to treat infections);
  - tramadol (a painkiller belonging to the class of opiates);
  - theophylline (used in the treatment of asthma);
  - antihistamines (medicines to treat hayfever, itch, and other allergic reactions) that cause sleepiness (such as chlorphenamine);
  - medicines to lower sugar levels in your blood (such as insulin, sulphonylureas such as glyburide or glibenclamide, and meglitinides such as nateglinide or repaglinide);
  - medicines to help you to sleep (sedatives such as diazepam).
- Medicines to treat **depression** (such as desipramine, venlafaxine, imipramine, paroxetine, citalopram) or other mental health problems (such as risperidone, haloperidol, thioridazine);
- Some medicines used to treat **high blood pressure** (beta-blockers such as metoprolol, and clonidine, a centrally acting antihypertensive);
- Some medicines used to treat **irregular heart rhythm** (such as propafenone, flecainide);
- Some medicines used to treat cancer (such as cyclophospamide, ifosphamide, tamoxifen);
- Some medicines for **Parkinson's disease** (such as levodopa, amantadine or orphenadrine);
- Ticlopidine or clopidogrel, mainly used in the treatment of **heart disease or stroke**;
- Medicines used in the treatment of **HIV infection and AIDS**, such as efavirenz and ritonavir;
- Medicines used to treat **epilepsy** such as valproate, carbamazepine, phenytoin or phenobarbital.

Your doctor will closely monitor you for side effects and/or may need to adjust the dose of the other medicines or Mysimba.

Mysimba with alcohol
Excessive use of alcohol while being treated with Mysimba might increase the risk for fits (seizures), mental disorder events or might reduce alcohol tolerance. Your doctor may suggest you do not drink alcohol while you are taking Mysimba, or try to drink as little as possible. If you do drink a lot now, do not just stop suddenly, because that may put you at risk of having a fit.

Pregnancy and breast-feeding
Mysimba should not be used during pregnancy, or in women currently attempting to become pregnant, or while 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.

Driving and using machines
Ask your doctor for advice before you drive and operate machines since Mysimba might make you feel dizzy and sleepy which may weaken your ability to concentrate and react.

Do not drive, use any tools or machines, or perform dangerous activities until you know how this medicine affects you.

If you experience fainting, muscle weakness or fits during treatment, do not drive or use machines.

In case of doubt, check with your doctor, who might consider to interrupt the treatment depending on your situation.

Mysimba contains lactose (a type of sugar)
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 Mysimba

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

The initial dose is usually one tablet (8 mg naltrexone hydrochloride / 90 mg bupropion hydrochloride) once a day in the morning. The dose will be gradually adapted as follows:
- **Week 1:** One tablet once a day in the morning
- **Week 2:** Two tablets every day, one in the morning and one in the evening
- **Week 3:** Three tablets every day, two in the morning and one in the evening
- **Week 4 and onward:** Four tablets every day, two in the morning and two in the evening

The maximum recommended daily dose of Mysimba is two tablets taken twice a day.
After 16 weeks and each year after your treatment initiation, your doctor will evaluate whether you should continue to take Mysimba.

If you have problems with your **liver** or **kidney**, or if you are **older than 65**, and depending on the severity of your problems, your doctor may carefully consider whether this medicine is suitable for you or recommend that you take a different dose, and monitor you more closely for potential side effects. Your doctor may test your blood before initiating treatment with Mysimba if you have high blood sugar (diabetes) or if you are older than 65, so that your doctor can decide if you should take this medicine or if you need to take a different dose.

This medicine is for oral use. Swallow your tablets whole. Do not cut them, chew them or crush them. The tablets should preferably be taken with food.

If you take more Mysimba than you should
If you take too many tablets, you may be more likely to have a fit or other side effects similar to those described in section 4 below. **Do not delay,** contact your doctor or your nearest hospital emergency department immediately.

If you forget to take Mysimba
Skip the missed dose and take your next dose at the next usual time. Do not take a double dose to make up for a forgotten dose.

If you stop taking Mysimba
You may need to take Mysimba for at least 16 weeks to have its full effect. **Do not stop taking Mysimba without talking to your doctor first.**

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.

Serious side effects
Tell your doctor straight away, if you notice any of the following serious side effects:
- **Suicidal thoughts and feeling depressed**
  Frequency of the side effects suicide attempts, suicidal behavior, suicidal thoughts and feeling depressed are not known and cannot be estimated from the available data in people taking Mysimba.
  There have been reports of depression, suicidal thoughts, and suicide attempts during treatment with Mysimba. If you have thoughts about harming yourself or other distressing thoughts, or if you are depressed and notice that you feel worse or develop new symptoms, **contact your doctor or go to a hospital straight away.**
- **Fits (seizures):**
  Rare - may affect up to 1 in 1,000 people taking Mysimba with risk of having a fit.
  Symptoms of a fit include convulsions and usually loss of consciousness. Someone who has had a fit may be confused afterwards and may not remember what has happened. Fits are more likely if you take too much, if you take some other medicines or if you are at a higher than usual risk of fits (see section 2).
- **Erythema multiforme and Stevens Johnson Syndrome**
  Not known - frequency cannot be estimated from the available data in people taking Mysimba.
  Erythema multiforme is a severe condition of the skin that may affect the mouth and other parts of the body, with red, often itchy spots starting on the limbs. Stevens Johnson Syndrome is a rare skin condition with severe blisters and bleeding in the lips, eyes, mouth, nose and genitals.
- **Rhabdomyolysis**
  Not known - frequency cannot be estimated from the available data in people taking Mysimba.
  Rhabdomyolysis is an abnormal breakdown of muscle tissue which can lead to kidney problems. Symptoms include severe muscle cramps, muscle pain or muscle weakness.

Other side effects include:

Very common side effects (may affect more than 1 in 10 people):
- Feeling sick (nausea), being sick (vomiting)
- Constipation
- Headache

Common side effects (may affect up to 1 in 10 people):
- Anxiety
- Dizziness, feeling of dizziness or “spinning” (vertigo)
- Feeling shaky (tremor)
- Difficulty in sleeping (make sure you do not take Mysimba near to bedtime)
- Changes in the taste of food (dysgeusia), dry mouth
- Difficulty concentrating
- Feeling of tiredness (fatigue) and sleepiness, drowsiness or lack of energy (lethargy)
- Ringing in the ears (tinnitus)
- Fast or irregular heartbeat
- Hot flush
- Increased blood pressure (sometimes severe)
- Pain in the upper part of the abdomen
- Pain in the abdomen
- Excessive sweating (hyperhidrosis)
- Rash, itching (pruritus)
- Hair loss (alopecia)
- Irritability
- Feeling jittery

Uncommon side effects (may affect up to 1 in 100 people):
- Hives (uticaria)
- Hypersensitivity
- Abnormal dreams
- Feeling nervous, feeling spacey, tension, agitation, mood swings, Tremor of the head or a limb which increases when trying to perform a particular function (intention tremor)
- Balance disorder
- Loss of memory (amnesia), Tingling or numbness of the hands or feet
- Motion sickness
- Burping
- Abdominal discomfort
- Indigestion
- Inflammation of the gallbladder (cholecystitis)
- Increased creatinine levels in the blood (indicating loss of kidney function)
- Increased liver enzymes and bilirubin levels, liver disorders
- Difficulty in getting or keeping an erection
- Feeling abnormal, weakness (asthenia)
- Thirst, feeling hot
- Chest pain
- Increased appetite, weight gain

Rare side effects (may affect up to 1 in 1,000 people):
- Low amount of certain white blood cells (Lymphocyte count decreased)
- Decreased haematocrit (indicating loss of red blood cell volume)
- Swelling of eyelids, face, lips, tongue or throat, which can cause great difficulty in breathing (angioedema)
- Excessive loss of body water (dehydration)
- Hallucinations
- Fainting, almost fainting (presyncope), loss of consciousness
- Fits
- Passage of fresh blood through the anus usually in or with stool (haematochezia)
- Projection of an organ or the tissue encompassing an organ through the wall of the cavity that normally contains it (hernia)
- Toothache

- Dental caries, cavities
- Pain in the lower part of the abdomen
- Injury to the liver due to drug toxicity
- Jaw pain
- A disorder characterised by a sudden compelling urge to urinate (micturition urgency)
- Irregular menstrual cycle, vaginal bleeding, dryness of the female vulva and vagina
- Coldness of extremities (hands, feet)

Not known side effects (frequency cannot be estimated from the available data):
- Swollen glands in the neck, armpit or groin (lymphadenopathy)
- Mood disorders
- Irrational ideas (delusions)
- Psychosis
- Loss of sexual desire
- Feeling hostile
- Severe suspiciousness (paranoia)
- Aggression
- Attention disturbance
- Nightmares
- Confusion, disorientation
- Memory impairment
- Restlessness
- Muscle stiffness, uncontrolled movements, problems with walking or coordination
- Blurred vision, eye pain, eye irritation, eye swelling, watery eyes, increased sensitivity to light (photophobia)
- Ear pain, ear discomfort
- Fluctuating blood pressure
- Difficulty in breathing
- Nasal discomfort, congestion, runny nose, sneezing, sinus disorder
- Sore throat, disorder of the voice, cough, yawning
- Haemorrhoids, ulcer
- Diarrhoea
- Passing wind (flatulence)
- Hepatitis
- Acne
- Groin pain
- Muscle pain
- Joint pain
- Abnormally frequent urination, painful urination
- Chills
- Increased energy

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly (see details below). By reporting side effects you can help provide more information on the safety of this medicine.

United Kingdom
Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard
or search for MHRA Yellow Card in the Google Play or Apple App Store

Ireland
HPRA Pharmacovigilance
Website: www.hpra.ie

Malta
ADR Reporting
Website: www.medicinesauthority.gov.mt/adrportal

5. How to store Mysimba

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 30°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 protect the environment.

6. Contents of the pack and other information

What Mysimba contains
- **The active substances are** naltrexone hydrochloride and bupropion hydrochloride. Each tablet contains 8 milligrams of naltrexone hydrochloride, equivalent to 7.2 milligrams of naltrexone, and 90 milligrams of bupropion hydrochloride, equivalent to 78 milligrams of bupropion.
- **The other ingredients (excipients) are:**
- **Tablet core:** microcrystalline cellulose, hydroxypropyl cellulose, lactose anhydrous, lactose monohydrate (see section 2 "Mysimba contains lactose"), cysteine hydrochloride, crospovidone type A, magnesium stearate, hypromellose, edetate disodium, colloidal silicon dioxide, and indigo carmine aluminium lake (E132). **Film-coating:** poly(vinyl alcohol), titanium dioxide (E171), macrogol (3350), talc and indigo carmine aluminium lake (E132).

What Mysimba looks like and contents of the pack
Mysimba prolonged-release tablets are blue, biconvex, round tablets debossed with "NB-890" on one side. Mysimba is available in packs containing 28 or 112 tablets. Not all pack sizes may be marketed.

Marketing Authorisation Holder

Orexigen Therapeutics Ireland Limited
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Manufacturer

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For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

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Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.