Package leaflet: Information for the patient
Mysimba® 8 mg/90 mg prolonged-release tablets
(naltrexone hydrochloride/bupropion hydrochloride)

Your medicine is known as the above but will be referred to as Mysimba throughout the remainder of this leaflet.

▼ 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 end stage 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, panic attacks 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).
- If you are taking medicines for **depression**, the use of these medicines together with Mysimba can lead to serotonin syndrome, a potentially life-threatening condition (see "Other medicines and Mysimba" in this section and section 4.)

Brugada syndrome
- if you have a condition called Brugada syndrome (a rare hereditary syndrome that affects the heart rhythm) or if cardiac arrest or sudden death occurred in your family.

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 hay fever, 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 amitriptyline, desipramine, imipramine, venlafaxine, paroxetine, fluoxetine, citalopram, escitalopram) or other mental health problems (such as risperidone, haloperidol, thioridazine). Mysimba may interact with some medicines used for treatment of depression and you may experience a so-called serotonin syndrome. Symptoms are mental status changes (e.g. agitation, hallucinations, coma), and other effects, such as body temperature above 38°C, increase in heart rate, unstable blood pressure, and exaggeration of reflexes, muscular rigidity, lack of coordination and/ or gastrointestinal symptoms (e.g. nausea, vomiting, diarrhoea) (see section 4.)
- 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 may make other medicines less effective when taken at the same time:
- **If you take digoxin for your heart**

If this applies to you, tell your doctor. Your doctor may consider adjusting the dose of digoxin.

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 planning 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