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 can quickly identify new safety information. You can contribute by reporting any side effects you may experience. At the end of section 4, you will read how to do this.

Read the entire leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- Do you have any questions? Then contact your doctor or pharmacist.
- Do not pass this medicine on to others, as it has been prescribed only for you. It can be harmful to others, even if they have the same complaints as you.
- Do you experience any of the side effects listed in section 4? Or do you experience a side effect that is not listed in this leaflet? Then contact your doctor or pharmacist.

Contents of this leaflet

1. What is Mysimba and what is it used for?

Mysimba contains two active ingredients: naltrexone hydrochloride and bupropion hydrochloride and is used in obese adults or adults who are overweight to control their weight along with a calorie-restricted diet and physical exercise. This medicine works on areas in the brain areas involved in the regulation of food intake and energy expenditure.

Obesity in adults over 18 years is defined as a body mass index of 30 or higher, and overweight in adults over 18 years is defined as a body mass index of 27 or higher and less than 30. The body mass index is calculated as the weighted body weight (kg) divided by the measured height squared (m2).

Mysimba is approved for use in patients with an initial body mass index of 30 or higher. However, it can also be given to individuals with a body mass index between 27 and 30 if there are other weight-related conditions, such as controlled high blood pressure (hypertension), type 2 diabetes, or high blood lipid levels (fat).

Mysimba can 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 advise you to stop the treatment if you have not maintained the weight loss of at least 5 percent of your original body weight after 1 year

of treatment, or if there is concern about increased blood pressure, or if there are concerns regarding the safety or tolerability of this medicine.

2. When should you not take this medicine or be extra careful with it?

When should you not use this medicine?

- You are allergic to any of the substances in this medicine.These substances can be found in section 6
- You have abnormally high blood pressure (hypertension), which is not controlled by a medicine. You have a condition that causes seizures, or you have a history of seizures.
- You have a brain tumor. seizures.
- drinking alcohol, or
- You are usually a heavy drinker and you have just stopped are going to stop while using Mysimba. You have recently stopped using sedatives or medicines for the treatment of anxiety (especially benzodiazepines) or you are going to stop while you
- You have recently stopped using sedatives or medications for treatment of anxiety (particularly benzodiazepines) or you are going to stop this while you Mysimba use;
- You have or had a bipolar disorder (extreme mood swings);
- You are using other medicines that contain bupropion or naltrexone;
- You have an eating disorder or have had one in the past (e.g., bulimia, anorexia nervosa);
- You are currently dependent on opioids, or you are using opioids for the treatment of dependence (e.g., methadone or buprenorphine) or you are going through an acute withdrawal phase (cold turkey);
- You are using medicines for depression or Parkinson's disease called monoamine oxidase inhibitors (MAOIs), or you have taken them in the past 14 days. You have a severe liver condition.
- You have end-stage kidney disease.
- When should you be extra careful with this medicine?

Contact
your doctor or pharmacist before using this medicine. This is important because with some conditions you have a greater
This is important because with certain conditions you have a greater chance has on side effects (see also section 4.4).
If you feel depressed, have suicidal thoughts or have ever attempted suicide, had panic attacks or other psychological problems, inform your doctor about this before taking this medicine.

Seizures/convulsions
Mysimba can cause seizures (epileptic fits) in up to 1 in 1000 patients (see also section 4). You should your doctor before taking this medicine:

if you have had a serious head injury or head trauma.
if you regularly drink alcohol (see "What to watch out for with alcohol?")
if you regularly take medications that help you sleep (sedatives);
if you are currently dependent on or addicted to cocaine or other stimulants products;
if you have diabetes for which you use insulin or oral medications that can cause low blood sugar levels in your blood (hypoglycemia); or

if you are using medications that increase the risk of a seizure (see "Are you taking any other medicines?").

If you have a seizure (epileptic fit), you should stop using Mysimba and contact your doctor immediately.

Hypersensitivity reactions
You should stop using Mysimba immediately and consult your doctor if you experience symptoms of an allergic reaction such as swelling of the throat, tongue, lips, or face, difficulty swallowing or breathing, dizziness, fever, rash, joint or muscle pain, itching or hives after taking this medicine (see also section 4).

Serious skin reactions have been reported in connection with treatment with Mysimba, including Stevens-Johnson syndrome and acute generalized exanthematous pustulosis (AGEP). Stop using Mysimba and seek immediate medical attention if you experience one or more of the symptoms associated with these serious skin reactions. A description of them can be found in section 4.

You should talk to your doctor, especially if:
- you have high blood pressure before taking Mysimba, as this may worsen. Your blood pressure and heart rate will be measured before you start taking Mysimba and while you are on it. If your blood pressure or heart rate increases significantly, you may need to stop using Mysimba.
- if you have uncontrolled coronary artery disease (a heart condition due to poor blood supply in the heart's blood vessels) with symptoms such as angina (chest pain) or a recent heart attack.
- you already have (or have had) a condition of the blood circulation of the brain (cerebrovascular condition).
- if you have liver problems before starting Mysimba.
- if you have kidney problems before starting Mysimba.
- if you have a history of mania (feeling very elated and excessively excited with unusual behavior).
- If you are taking medications for depression, the concurrent use of these medications with Mysimba can lead to serotonin syndrome. This condition can be life-threatening (see 'Are you taking any other medicines?' in this section and section 4.)

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

Elderly
Be cautious with the use of Mysimba if you are 65 years or older. Mysimba is not recommended if you are older than 75 years.

Children and adolescents up to 18 years
No studies have been conducted in children and adolescents under 18 years. Therefore, naltrexone/bupropion should not be used in children and adolescents under 18 years.

Are you taking any other medicines?
Are you taking any other medicines besides Mysimba, or have you recently taken any or is there a possibility that you will take other medicines in the near future? Then tell your doctor or pharmacist.

Do not take Mysimba with:

- Monoamine oxidase inhibitors (medicines for the treatment of depression or Parkinson's disease) such as phenelzine, selegiline, or rasagiline. You should stop at least 14 days before starting with Parkinson) such as phenelzine, selegiline, or rasagiline. You should stop at least 14 days before starting Mysimba with these medications to stop (see "When should you not use this medicine?")
- Opioid-containing medications such as cough and cold remedies (such as mixtures with dextromethorphan or codeine), opioid addiction (such as methadone or buprenorphine), pain (e.g. tramadol, morphine or codeine), diarrhea (e.g. analgesic). You must have stopped using opioid-like medications at least 7 to 10 days prior to starting Mysimba. Your doctor can perform a test to ensure that your body is free of these substances before you begin your treatment.
  If you need treatment with opioids (for example, during surgery) while you are using Mysimba, you must stop taking Mysimba at least 3 days before starting treatment with opioids or a surgical procedure. Naltrexone contained in Mysimba blocks the effects of opioids for several days after you stop taking Mysimba.
  Taking Mysimba together with medicines for the treatment of depression and opioids can cause serious life-threatening reactions, such as serotonin syndrome and seizures (see section 2. Tell your doctor if...), (see "Possible side effects"). doctor as...), (see "Possible side effects"). you take higher doses of opioids to overcome this effect of naltrexone, you may experience acute opioid intoxication, which can be life-threatening. After stopping Mysimba, you may be more sensitive to low doses of opioids (see "When should you not use this medicine"). Tell

your doctor if you are using any of the following medications, your doctor will carefully monitor you for side effects Medications that, alone or in combination with naltrexone/bupropion, increase the risk of seizures, such as:

- medications for depression and other mental health problems; increase, such as:
  - inhalers for respiratory disorders, such as asthma);
  - medications for the prevention of malaria; quinolones (antibiotics such as ciprofloxacin for the treatment of infections);
  - medications for the prevention of malaria;
  - quinolones (antibiotics such as ciprofloxacin for the treatment of infections);
  - theophylline (used in the treatment of asthma);
  - antihistamines (medicines for hay fever, itching, and other allergic reactions) that cause drowsiness (such as chlorphenamine);
  - medicines that lower the sugar levels in your blood (such as insulin, sulfonylureas such as glyburide or glibenclamide and meglitinides such as nateglinide or repaglinide);
  - medicines that help you sleep (sedatives such as diazepam).
- Medicines for the treatment of depression (such as amitriptyline, desipramine, imipramine, venlafaxine, paroxetine, fluoxetine, citalopram, escitalopram) or other mental health

problems (such as risperidone, haloperidol, thioridazine). Mysimba and some medicines that are used to treat depression can affect each other. You may develop a so-called serotonin syndrome. Symptoms include changes in mental state (e.g. agitation, seeing, hearing, or feeling things that are not there [hallucinations], coma) and other effects, such as body temperature above 38 °C, increased heart rate, unstable blood pressure and increased reflexes, muscle stiffness, lack of coordination and/or gastrointestinal complaints (e.g. nausea, vomiting, diarrhea) (see section 4).

- Some medications for the treatment of high blood pressure (beta-blockers such as metoprolol and clonidine, a centrally acting antihypertensive);
- Some medications for the treatment of irregularheart rhythm (such as propafenone, flecainide);
- Some medications for the treatment of cancer (such as cyclophosphamide, ifosfamide, tamoxifen);
- Some medications for the treatment of Parkinson's disease (such as levodopa, amantadine or orphenadrine);
- Ticlopidine or clopidogrel, mainly used for the treatment of a heart condition or stroke;
- Medications used for the treatment of HIV infection and AIDS, such as efavirenz and ritonavir;
- Medicines used for the treatment of epilepsy such as valproate, carbamazepine, phenytoin or phenobarbital.

Your doctor will closely monitor you for side effects and/or possibly adjust the dose of the other medicine or Mysimba.

Mysimba can make other medicines less effective when taken at the same time: if you use digoxin for your heart

- if you are using digoxin for your heart

this applies to you, tell your doctor. if this applies to you, tell your doctor. doctor may consi der adjusting the dose of digoxin.adjust the dose of digoxin.

What should you watch out for with alcohol?
Excessive use of alcohol during treatment with Mysimba can increase the risk ofseizures (epileptic attacks) or mental disorders or reduce thetolerance for alcohol. Your doctor may suggest that you do not drink alcohol during yourtreatment with Mysimba, or drink as little as possible. If you currently drink a lot, do not stop suddenly, becausethat poses a risk for a seizure.

Pregnancy and breastfeeding
Mysimba should not be used during pregnancy or breastfeeding or by women who arebreastfeeding. at that moment plan to become pregnant.
Are you pregnant, do you think you are pregnant to be, do you want to become pregnant or are you breastfeeding? Then contact your doctor or pharmacist before using this medicine. Driving ability

and the use of machinesConsult
your doctor before driving or operating machines because Mysimba can make you dizzy ordrowsy, which may impair your ability to concentrate and react. Do not drive, use tools, operate machines, or perform

hazardous activitiesuntil you know how this medicine affects you. until you know how this medicine affects you.

you faint, experience muscle weakness, or have a seizure during the trea you faint, experience muscle weakness, or have a seizure during the treadizziness, do not drive and do not operate machinery.

Consult your doctor in case of doubt. Your doctor can then considerdepending on your situation, interrupting the treatment.

Mysimba contains lactose (a type of sugar)

If your doctor has told you that you cannot tolerate certain sugars,contact your doctor before taking this medicine.

3. How to take this medicine?

Always take this medicine exactly as your doctor or pharmacist hastold you. If you are unsure about the correct use? Then contact your doctor or pharmacist.

The initial dose is usually one tablet (8 mg naltrexone hydrochloride / 90 mg bupropion hydrochloride) once daily in the morning. The dose should be gradually ad justed: Week 1: one tablet once

- daily in the morning. Week 2: two tablets per day,
- one in the one 's Week 3: three tablets per day,
- two in the morning. in the morning and one in the evening.
- Week 4 and beyond: four tablets per day, two in the morning and two in the evening.

The maximum recommended daily dose of Mysimba is four tablets, taken as two tablets twice a day.
After 16 weeks and each year after starting your treatment, the doctor will assess whether you should continue using Mysimba.

If you have liver or kidney problems, or if you are over 65years old, and depending on the severity of your problems, your doctor will carefully consider whether this medication is suitable for you or advise you to take a different dose and monitor you closelyfor possible side effects. If you have high blood sugar (diabetes) or if you are over 65 then your doctor may do blood tests to decide whether you should use this medicine or take a different dose.

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

Have you taken too much of this medicine?
If you have taken too many tablets, you have a higher chance of aseizure or other side effects as described in section 4 below. Do not delay, contactyour doctor or the doctor or the emergency department of the nearest hospital.

Did you forget to take this medicine to take?
Skip the missed dose and take the next tablet at the usual time. Do not take a doubledose to make up for a missed dose. to make up a missed dose.

you stop taking this medicine You must take Mysimba for at least 16 weeks for the full effect. Do not stop taking
Mysimba before you have spoken withyour doctor. Do you have any other questions about the use of this medicine? Then contact

Do you have any other questions about the use of this medicine? doctor your doctor or pharmacist.

4. Possible side effects

Like any medicine can this medicine also have side effects, although not everyone gets them. to deal with.

Serious side effects
Tell your doctor immediately if you notice any of the following serious side effects:

- Suicidal thoughts and depression
  Frequency of side effects attempt to suicide, suicidal behavior, suicidal thoughts and depression is not known and can not be determined with theavailable data on people using Mysimba.
  There have been reports of depression, thoughts of and suicide attempts during treatment with Mysimba. If you are thinking about harming yourselfor if you have other disturbing thoughts, or if you are depressed andnotice that you feel worse or develop new symptoms, contactyour doctor or go straight to a hospital.
- Seizures (epileptic fits):
  Rare - may occur in up to 1 in 1000 peopleusing Mysimba with a risk of seizures. Symptoms of a seizure include convulsions and usually loss ofconsciousness. Someone who has had a seizure may have afterwards be confused and may not remember what happened. There isa greater chance of a seizure if you take too much, if you take the drug with certain other medications or if you have a higher risk of having seizures (see section 2). Erythema multiforme and Stevens-Johnson syndrome
- Unknown – frequency
  cannot be determined with the available data on peopleusing Mysimba. Erythema multiforme is a serious skin condition
  that affects the mouth and other parts of the body can affect, with red, often itchy spots encounter, with red, often itchy spots bbeginning on arms and legs. The Stevens-Johnson syndrome is a rare skincondition with severe blisters and bleeding of the lips, eyes, mouth, nose, and genitals.
- Acute generalized exanthematous pustulosis
  Unknown – frequency cannot be determined with the available data on people using Mysimba. A red, scaly, widespread skin rash with bumps under the skin and blisters, accompanied by fever. Symptoms usually occur at the start of the treatment.
- Rhabdomyolysis

Unknown - frequency cannot be determined with the available data on people who use Mysimba.
Rhabdomyolysis is the abnormal breakdown of muscle tissue which can lead to kidney problems. Symptoms include severe muscle cramps, muscle pain, or muscle weakness.

- Lupus rash or worsening of symptoms related to lupus
  Unknown - frequency can not be determined with the available data on people using Mysimba.
  Lupus is a disorder of the immune system that affects the skin and other organs. If you experience lupus flare-ups, rash, or skin lesions (especially in areas that are exposed to sunlight) while using Mysimba, contact your doctor immediately; treatment may need to be stopped.
- Serotonin syndrome that may manifest as a change in mental state(e.g. agitation, seeing, hearing, or feeling things that are not there [hallucinations], coma) and other symptoms, such as body temperature above 38 °C, increased heartrate, unstable blood pressure and increased reflexes, muscle stiffness, lack of coordinationand/or gastrointestinal symptoms (e.g. nausea, vomiting, diarrhea) when Mysimba is takensimultaneously with medicines for the treatment of depression (such as paroxetine, citalopram, escitalopram, fluoxetine and venlafaxine and opioids (see section 2).
  Unknown – frequency cannot be determined with theavailable data on people using Mysimba)

Other side effects include:

Very common side effects (may occur in more than 1 in 10 people)
- Nausea or 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)
- Sleep problems (do not take Mysimba just before going to bed)
- Changes in the taste of food (dysgeusia), dry mouth
- Difficulty concentrating
- Fatigue and drowsiness, sleepiness or lack of energy (lethargy)
- Ringing in the ears (tinnitus)
- Rapid or irregular heartbeat
- Hot flashes
- High blood pressure (sometimes severe)
- Upper abdominal pain
- Abdominal pain
- Excessive sweating (hyperhidrosis)
- Rash, itching (pruritus)
- Hair loss (alopecia)
- Irritability
- Nervousness

Uncommon side effects (may occur in up to 1 in 100 people)
- Hives (urticaria)
- Hypersensitivity
- Abnormal dreams
- Nervousness, lightheadedness, tension, agitation, mood swings
- Involuntary shaking of the head or a limb that worsens when trying to perform a specific function (intention tremor)
- Balance disorder
- Memory loss (amnesia)
- Tingling sensation or numbness in hands or feet
- Motion sickness
- Belching
- Abdominal discomfort
- Indigestion
- Inflammation of the gallbladder (cholecystitis)
- Increased creatinine levels in the blood (indicating a loss of kidney function)
- Increased liver enzymes and bilirubin levels, liver disorders
- Difficulty getting or maintaining an erection
- Abnormal sensation, weakness (asthenia)
- Thirst, feeling warm
- Chest pain
- Increased appetite, weight gain

Rare side effects (may occur in up to 1 in 1,000 people)
- Low count of a certain type of white blood cells (reduced lymphocyte count)
- Decreased hematocrit (indicating a reduction in the number of red blood cells)
- Swollen eyelids, face, lips, tongue, or throat, which can lead to severe breathing problems (angioedema)
- Excessive loss of body fluid (dehydration)
- Hallucinations
- Fainting, loss of consciousness, near fainting (presyncope)
- Seizures
- Loss of fresh blood via the anus usually in or with stool (hematochezia)
- Protrusion of an organ or organ tissue through a hole in the abdominal wall that normal spoken content (hernia)
- Toothache
- Dental caries, cavities
- Pain in the lower abdomen
- Liver damage due to drug toxicity
- Jaw pain
- A disorder characterized by a suddenurgent need to urinate (urge to urinate)
- Irregular menstrual cycle, vaginal bleeding, dryness of the vulva and vagina
- Cold hands and feet

Not known (can not be determined from the available data)
- Swollen glands in the neck, armpit, or groin (lymphadenopathy)

- Mood disorder
- Irrational thoughts (delusions)
- Psychosis
- Sudden feeling of intense fear (panic attack)
- Loss of sexual desire
- Hostility
- Severe suspicion (paranoia)
- Aggression
- Attention disorder
- Nightmares
- Confusion, disorientation
- Memory disorder
- Restlessness
- Stiff muscles, 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
- Breathing problems
- Nasal discomfort, blocked nose, runny nose, sneezing, sinus disorder
- Sore throat, voice disorder, coughing, yawning
- Hemorrhoids, ulcers
- Diarrhea
- Flatulence
- Liver inflammation (hepatitis)
- (Youth) acne
- Pain in the groin
- Muscle pain
- Joint pain
- Abnormally frequent urination, pain during urination
- Chills
- Increase in energy

Reporting side effects
If you experience side effects, contact your doctor or pharmacist. This also applies to possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system as mentioned in Appendix V. By reporting side effects, you can help us obtain more information about the safety of this medicine.

5. How do you store this medicine?

Keep out of the sight and reach of children.

Do not use this medicine after the expiry date. It is found on the box and the strip after EXP. It includes a month and a year. The last day of that month is the expiry date.

Store below 30°C.

Do not flush medicines down the sink or toilet and do not throw them in the trash. Ask your pharmacist what to do with medicines you no longer use. They will be destroyed in a responsible manner and will not enter the environment.

6. Contents of the package and other information

What substances are in this medicine?

- The active substances in this medicine are naltrexone hydrochlorideand bupropion hydrochloride. Each tablet contains 8 milligrams of naltrexone hydrochloride, equivalent to 7,2 milligrams of naltrexone, and 90 mg of bupropion hydrochloride, equivalent to 78 mg of bupropion.
- The other ingredients in this medicine are:
  Tablet core: microcrystalline cellulose, hydroxypropyl cellulose, anhydrouslactose, lactose monohydrate (see section 2 "Mysimba containslactose"), cysteine hydrochloride, crospovidone type A, magnesium stearate, hypromellose,disodium edetate, colloidal silicon dioxide and indigo carmine aluminum lake (E132). Film coating: poly(vinylalcohol), titanium dioxide (E171), macrogol (3350), talc, and indigo carmine aluminum lake (E132).

What does Mysimba look like and how many are in a package?
Mysimba prolonged-release tablets are blue, biconvex, round tablets with "NB890" engraved on one side. Mysimba is available in packages of 28, 112 tablets. Not all mentionedpackage sizes are marketed. marketed. marketed. marketed.

Patient card: how to handle the information
In the package of Mysimba, you will find a patient card with importantsafety information for you and your doctors. Always carry the patient card with you.

Marketing authorization holder and marketed. marketed. manufacturer

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This leaflet was last approved in .

Other sources of information

More information about this medicine is available on the website of the European Medicines Agency: http://www.ema.europa.eu.