PATIENT INFORMATION LEAFLET

SCHEDULING STATUS

S5

CONTRAVE, 8 mg/90 mg prolonged release tablets.

Naltrexone hydrochloride and bupropion hydrochloride

Contains sugar:

lactose monohydrate 30 mg/tablet

lactose anhydrous 45,5 mg/tablet.

Read all of this leaflet carefully before you start taking CONTRAVE

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- Contrave has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What Contrave is and what it is used for
2. What you need to know before you take Contrave
3. How to take Contrave
4. Possible side effects
5. How to store Contrave
6. Contents of the pack and other information

1. What Contrave is and what it is used for

Contrave contains 2 active ingredients: 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).

Contrave 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 Contrave

Do not take Contrave:

- if you are hypersensitive (allergic) to naltrexone, to bupropion or to any of the other ingredients Contrave (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 Contrave;
- 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 Contrave;
- if you have 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;
- if you are under 18 years of age.

Warnings and precautions

Talk to your doctor or healthcare provider before taking Contrave:

- if you feel depressed, consider suicide, have a history of attempting suicide, panic attacks or any other mental health problems, you should inform your doctor before taking this medicine
- if you have seizures (fits). Contrave has been shown to cause fits in up to 1 in 1000 patients (see section 4). If you have a fit (seizure), you should stop taking Contrave and consult your doctor immediately
- if you have had a serious head injury or head trauma
- if you regularly drink alcohol (see "Contrave 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 and use insulin or oral medicines that may lower sugar levels in your blood (hypoglycaemia)
- if you have a heart condition and are currently taking medicines such as digoxin
- if you are taking medicines that may increase the risk of fits (see "Other medicines and Contrave").

You should stop taking Contrave 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 if:

- you have high blood pressure before taking Contrave, because it can become worse. You will have your blood pressure and heart rate measured before you start taking Contrave and while you are taking it. If your blood pressure or heart rate increases significantly, you may need to stop taking Contrave.
- 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 Contrave.
- you have any kidney problems before you start Contrave.
- 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 CONTRAVE can lead to serotonin syndrome, a potentially life-threatening condition (see “Other medicines and CONTRAVE” 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 Contrave, if you are 65 years or older. Contrave 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 Contrave should not be used in children and adolescents below 18 years.

Other medicines and Contrave

Do not take Contrave 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 Contrave (see "Do not take Contrave").
- 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, peregoric). You must have stopped taking any opiate medicines at least 7-10 days before starting Contrave. 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 Contrave you may be more sensitive to low doses of opiates (see "Do not take Contrave").

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 ciprofloxacin 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 amitriptyline, desipramine, imipramine, venlafaxine, paroxetine, fluoxetine, citalopram, escitalopram) or other mental health problems (such as risperidone, haloperidol, thioridazine). CONTRAVE 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 CONTRAVE.

CONTRAVE 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.

Contrave with alcohol

Excessive use of alcohol while being treated with Contrave 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 Contrave, 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

Contrave should not be used during pregnancy, 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 Contrave 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.

Contrave contains lactose

Patients with the rare hereditary conditions of lactose/frucose or galactose intolerance should not take Contrave.

3. How to take Contrave

Do not share medicines prescribed for you with any other person.

Always take Contrave 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, once a day in the morning. The dose will be gradually changed as follows:

- **Week 1:** One tablet once a day in the morning
- **Week 2:** One tablet twice a 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:** Two tablets twice a day, two in the morning and two in the evening

The maximum recommended daily dose of Contrave is two tablets taken twice a day.

Your doctor will tell you how long your treatment with Contrave will last. After 16 weeks and each year after your treatment initiation, your doctor will evaluate whether you should continue to take Contrave. If you have the impression that the effect of Contrave is too strong or too weak, tell your doctor or pharmacist.

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 Contrave 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 Contrave than you should

In the event of overdosage, consult your doctor or pharmacist immediately. If netiher is available, contact the nearest hospital or poison centre. 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.

If you forget to take Contrave

Do not take a double dose to make up for forgotten individual doses.

If you stop taking Contrave

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

4. Possible side effects

Contrave can have side effects.

Not all side effects reported for Contrave are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking Contrave, please consult your healthcare provided for advice.

If any of the following happens, stop taking Contrave and tell your doctor immediately or go to the casualty department at your nearest hospital:

- 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 CONTRAVE.

- Fits (seizures): 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 CONTRAVE. 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 CONTRAVE. Rhabdomyolysis is an abnormal breakdown of muscle tissue which can lead to kidney problems. Symptoms include severe muscle cramps, muscle pain or muscle weakness.
  - Lupus skin rash or worsening of lupus symptoms

  Not known - frequency cannot be estimated from the available data in people taking CONTRAVE. Lupus is an immune system disorder affecting the skin and other organs. If you experience lupus flares, skin rash or lesions (particularly on sun-exposed areas) while taking CONTRAVE, contact your doctor straight away, as it might be necessary to stop the treatment.
  - Serotonin syndrome, that can manifest as 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), while taking CONTRAVE together with medicines used for treatment of depression (such as paroxetine, citalopram, escitalopram, fluoxetine and venlafaxine (see section 2.)

Not known - frequency cannot be estimated from the available data in people taking CONTRAVE)

- swelling of eyelids, face, lips, tongue or throat, which can cause great difficulty in breathing (angioedema), sudden life-threatening allergic reaction (anaphylactic shock).

These are very serious side effects. If you experience these, you may have had a serious reaction to Contrave. You may need urgent medical attention or hospitalisation.

Tell your doctor if you notice any of the following:

frequent side effects:

- feeling sick (nausea), being sick (vomiting),
- pain in the abdomen,
- constipation,
- headache,
- difficulty in sleeping (make sure you do not take Contrave close to bedtime),
- anxiety, agitation,
- joint and muscle pain,
- low amount of certain white blood cells (lymphocyte count decreased),
- dizziness, feeling of dizziness or “spinning” (vertigo),
- feeling shaky (tremor),
- increased energy, irritability,
- feeling depressed, mood disorders,
- chills, fever,
- decreased appetite, diarrhoea,
- changes in the taste of food (dysgeusia), dry mouth, toothache,
- 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,

- watery eyes,
- pain in the upper part of the abdomen,
- delayed ejaculation,
- chest pain, change to electrocardiogram (record of the electrical activity of the heart),
- excessive sweating (hyperhidrosis),
- hives, rash, itching (pruritus),
- hair loss (alopecia).

Less frequent side effects:

- cold sores (oral herpes),
- itching, blisters, cracking, and scaling of the skin between the toes (athlete's foot or tinea pedis),
- swollen glands in the neck, armpit or groin (lymphadenopathy),
- excessive loss of body water (dehydration),
- loss of appetite (anorexia),
- increased appetite, weight gain,
- abnormal dreams, nightmares,
- flushing,
- feeling nervous, feeling spacey, tension, agitation, mood swings, hallucinations, confusion, severe suspiciousness (paranoia), disorientation,
- loss of sexual desire,
- tremor of the head or a limb which increases when trying to perform a particular function (intention tremor),
- balance disorder,
- loss of memory (amnesia), mental impairment,
- almost fainting (presyncope),
- motion sickness,
- ear pain, ear discomfort,

- visual disturbances, blurred vision, eye irritation, pain or swelling, increased sensitivity to light (photophobia),
- nasal discomfort, congestion, runny nose, sneezing, sinus disorder,
- sore throat, increase in mucus that is coughed up, difficulty in breathing, disorder of the voice, cough, yawning,
- fluctuating or increased blood pressure (sometimes severe),
- pain in the lower part of the abdomen,
- burping,
- swelling of the lips,
- 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),
- passing wind (flatulence), haemorrhoids, ulcer, cavities,
- inflammation of the gallbladder (cholecystitis),
- a problem with the spine where supporting disc between two bones (vertebra) bulges out (intervertebral disc protrusion),
- jaw and groin pain,
- a disorder characterised by a sudden compelling urge to urinate (micturition urgency), abnormally frequent urination, painful urination,
- irregular menstrual cycle, vaginal bleeding, dryness of the female vulva and vagina,
- difficulty in getting or keeping an erection,
- feeling abnormal, weakness (asthenia),
- thirst, feeling hot,
- coldness of extremities (hands, feet),
- increased creatinine levels in the blood (indicating loss of kidney function),
- increased liver enzymes and bilirubin levels, liver disorders, hepatitis
- decreased haematocrit (indicating loss of red blood cell volume)
- acne, oily skin,

- unusual bleeding or bruising under the skin,
- changes in blood sugar levels,
- feeling irritable or hostile,
- suicidal thoughts, suicide attempts, feeling of observing yourself from outside your body or sense of unreality of surroundings (depersonalisation),
- muscle stiffness, uncontrolled movements, problems with walking or coordination,
- memory impairment,
- fainting, loss of consciousness,
- tingling or numbness of the hands or feet,
- widening of blood vessels, low blood pressure when you stand up from sitting or lying down (postural hypotension),
- your skin or the whites of your eyes turning yellow (jaundice),
- erythema multiforme (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 (a rare skin condition with severe blisters and bleeding in the lips, eyes, mouth, nose and genitals),
- worsening of psoriasis (thickened patches of red skin),
- muscle twitching,
- urinary retention,
- fixed, irrational ideas (delusions), aggression,

abnormal muscle breakdown which can lead to kidney problems (rhabdomyolysis).

Frequency cannot be estimated for the following side effects:

- psychosis,
- abdominal discomfort,
- indigestion,
- rash,
- an inflammatory disease caused when the immune system attacks its own tissues (lupus)

- increased blood pressure
- Feeling of acute and disabling anxiety (panic attack)

Reporting of side effects

If you get side effects, talk to your doctor of pharmacist. You can also report side effects to SAHPRA via the "6.04 Adverse Drug Reaction Reporting Form", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/index/8. By reporting side effects, you can provide more information on the safety of Contrave.

Alternately you can contact Acino Pharma (Pty) Ltd at +27 11 516 1700.

Website: www.acino.co.za.

5. How to store Contrave

Store all medicines out of reach of children.

Store at or below 30 °C.

Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What Contrave 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**: magnesium stearate, lactose anhydrous, lactose monohydrate, crospovidone type A, FD & C Blue #2 aluminium lake, hypromellose, edetate disodium, colloidal silicone dioxide, polyvinyl alcohol, titanium dioxide, macrogol 3350 and talc.

What Contrave looks like and contents of the pack

Contrave prolonged-release tablets are blue, biconvex, round tablets debossed with “NB-890” on one side. Contrave is available in packs containing 112 tablets.

Holder of Certificate of Registration

Acino Pharma (Pty) Ltd

106 16th Road

Midrand,

1686

This leaflet was last revised in

25 April 2023

Registration number

52/11.3/0478

Registration No.: Namibia (NS3): 20/32.2/0114