MEDICATION GUIDE

CONTRAVE® (CON-trayv)

(naltrexone HCl and bupropion HCl) extended-release tablets

What is the most important information I should know about CONTRAVE?

CONTRAVE can cause serious side effects, including:

- **Suicidal thoughts or actions.** One of the ingredients in CONTRAVE is bupropion. Bupropion has caused some people to have suicidal thoughts or actions or unusual changes in behavior, whether or not they are taking medicines used to treat depression.

  Bupropion may increase suicidal thoughts or actions in some children, teenagers, and young adults within the first few months of treatment.

  If you already have depression or other mental illnesses, taking bupropion may cause it to get worse, especially within the first few months of treatment.

  Stop taking CONTRAVE and call a healthcare provider right away if you, or your family member, have any of the following symptoms, especially if they are new, worse, or worry you:

  - thoughts about suicide or dying
  - attempts to commit suicide
  - new or worse depression
  - new or worse anxiety
  - feeling very agitated or restless
  - panic attacks
  - new or worse irritability
  - acting aggressive, being angry, or violent
  - acting on dangerous impulses
  - an extreme increase in activity and talking (mania)
  - other unusual changes in behavior or mood
  - trouble sleeping (insomnia)

  While taking CONTRAVE, you or your family members should:

  - Pay close attention to any changes, especially sudden changes, in mood, behaviors, thoughts, or feelings. This is very important when you start taking CONTRAVE or when your dose changes.
  - Keep all follow-up visits with your healthcare provider as scheduled. Call your healthcare provider between visits as needed, especially if you have concerns about symptoms.

CONTRAVE has not been studied in and is not approved for use in children under the age of 18.

What is CONTRAVE?

CONTRAVE is a prescription medicine which contains 2 medicines (naltrexone and bupropion) that may help some obese or overweight adults, who also have weight related medical problems, lose weight and keep the weight off.

CONTRAVE should be used with a reduced calorie diet and increased physical activity.

It is not known if CONTRAVE changes your risk of heart problems or stroke or of death due to heart problems or stroke.

It is not known if CONTRAVE is safe and effective when taken with other prescription, over-the-counter, or herbal weight loss products.

It is not known if CONTRAVE is safe and effective in children under 18 years of age.

CONTRAVE is not approved to treat depression or other mental illnesses, or to help people quit smoking (smoking cessation). One of the ingredients in CONTRAVE, bupropion, is the same ingredient in some other medicines used to treat depression and to help people quit smoking.

Do not take CONTRAVE if you:

- have uncontrolled hypertension.
- have or have had seizures.
- use other medicines that contain bupropion such as WELLBUTRIN, WELLBUTRIN SR, WELLBUTRIN XL, APLENZIN and ZYBAN.
- have or have had an eating disorder called anorexia (eating very little) or bulimia (eating too much and vomiting to avoid gaining weight).
- are dependent on opioid pain medicines or use medicines to help stop taking opioids such as methadone or buprenorphine, or are in opiate withdrawal.
- drink a lot of alcohol and abruptly stop drinking, or use medicines called sedatives (these make you sleepy), benzodiazepines, or anti-seizure medicines and you stop using them all of a sudden.
- are taking medicines called monoamine oxidase inhibitors (MAOIs). Ask your healthcare provider or pharmacist if you are not sure if you take an MAOI, including linezolid. **Do not** start CONTRAVE until you have stopped taking your MAOI for at least 14 days.
- are allergic to naltrexone or bupropion or any of the ingredients in CONTRAVE. See the end of this Medication Guide for a complete list of ingredients in CONTRAVE.

- are pregnant or planning to become pregnant. Tell your healthcare provider right away if you become pregnant while taking CONTRAVE.

Before taking CONTRAVE, tell your healthcare provider about all of your medical conditions, including if you:

- have or have had depression or other mental illnesses (such as bipolar disorder)
- have attempted suicide in the past
- have or have had seizures
- have had a head injury
- have had a tumor or infection of your brain or spine (central nervous system)
- have had a problem with low blood sugar (hypoglycemia) or low levels of sodium in your blood (hyponatremia)
- have or have had liver problems
- have high blood pressure
- have or have had a heart attack, heart problems, or have had a stroke
- have kidney problems
- are diabetic taking insulin or other medicines to control your blood sugar
- have or have had an eating disorder
- drink a lot of alcohol
- abuse prescription medicines or street drugs
- are over the age of 65
- are breastfeeding or plan to breastfeed. CONTRAVE can pass into your breast milk and may harm your baby. You and your healthcare provider should decide if you should take CONTRAVE or breastfeed. You should not do both.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

CONTRAVE may affect the way other medicines work and other medicines may affect the way CONTRAVE works causing side effects.

Ask your healthcare provider for a list of these medicines if you are not sure.

Know the medicines you take. Keep a list of them to show your healthcare provider or pharmacist when you get a new medicine.

How should I take CONTRAVE?

How to take CONTRAVE		
	Morning Dose	**Evening Dose**
Starting: Week 1	1 tablet	None
Week 2	1 tablet	1 tablet
Week 3	2 tablets	1 tablet
Week 4 Onward	2 tablets	2 tablets

- Take CONTRAVE exactly as your healthcare provider tells you to.
- **Do not** change your CONTRAVE dose without talking with your healthcare provider.
- Your healthcare provider will change your dose if needed.
- Your healthcare provider should tell you to stop taking CONTRAVE if you have not lost a certain amount of weight after 16 weeks of treatment.
- **Swallow CONTRAVE tablets whole. Do not cut, chew, or crush CONTRAVE tablets**. Tell your healthcare provider if you cannot swallow CONTRAVE tablets whole.
- **Do not** take more than 2 tablets in the morning and 2 tablets in the evening.
- **Do not** take more than 2 tablets at the same time or more than 4 tablets in 1 day.
- **Do not** take CONTRAVE with high-fat meals. It may increase your risk of seizures.
- If you miss a dose of CONTRAVE, wait until your next regular time to take it. **Do not** take more than 1 dose of CONTRAVE at a time.
- If you take too much CONTRAVE, call your healthcare provider or go to the nearest emergency room right away.

What should I avoid while taking CONTRAVE?

- **Do not** drink a lot of alcohol while taking CONTRAVE. If you drink a lot of alcohol, talk with your healthcare provider before suddenly stopping. If you suddenly stop drinking alcohol, you may increase your chance of having a seizure.

What are the possible side effects of CONTRAVE?

CONTRAVE may cause serious side effects, including:

- **See "What is the most important information I should know about CONTRAVE?"**
- **Seizures.** There is a risk of having a seizure when you take CONTRAVE. The risk of seizure is higher in people who:
  - o take higher doses of CONTRAVE
  - o have certain medical conditions
  - o take CONTRAVE with certain other medicines

  Do not take any other medicines while you are taking CONTRAVE unless your healthcare provider has said it is okay to take them.

  If you have a seizure while taking CONTRAVE, stop taking CONTRAVE and call your healthcare provider right away.

  You should not take CONTRAVE again if you have a seizure.
- **Risk of opioid overdose.** One of the ingredients in CONTRAVE (naltrexone) can increase your chance of having an opioid overdose if you take opioid medicines while taking CONTRAVE.

  You can accidentally overdose in 2 ways:
  - o Naltrexone blocks the effects of opioids, such as heroin, methadone or opioid pain medicines. **Do not** take large amounts of opioids, including opioid-containing medicines, such as heroin or prescription pain pills, to try to overcome the opioid-blocking effects of naltrexone. This can lead to serious injury, coma, or death.
  - o After you take naltrexone, its blocking effect slowly decreases and completely goes away over time. If you have used opioid street drugs or opioid-containing medicines in the past, using opioids in amounts that you used before treatment with naltrexone can lead to overdose and death. You may also be more sensitive to the effects of lower amounts of opioids:
    - after you have gone through detoxification
    - when your next dose of CONTRAVE is due
    - if you miss a dose of CONTRAVE
    - after you stop CONTRAVE treatment

  It is important that you tell your family and the people closest to you of this increased sensitivity to opioids and the risk of overdose.

  You or someone close to you should get emergency medical help right away if you:
  - o have trouble breathing
  - o become very drowsy with slowed breathing
  - o have slow, shallow breathing (little chest movement with breathing)
  - o feel faint, very dizzy, confused, or have unusual symptoms
- **Sudden opioid withdrawal.** People who take CONTRAVE must not use any type of opioid (must be opioid-free) including street drugs, prescription pain medicines (including tramadol), cough, cold, or diarrhea medicines that contain opioids, or opioid dependence treatments, buprenorphine or methadone, **for at least 7 to 10 days before starting CONTRAVE.** Using opioids in the 7 to 10 days before you start taking CONTRAVE may cause you to suddenly have symptoms of opioid withdrawal when you take it. Sudden opioid withdrawal can be severe, and you may need to go to the hospital. Tell your healthcare provider you are taking CONTRAVE before a medical procedure or surgery.
- **Severe allergic reactions.** Some people have had a severe allergic reaction to bupropion, one of the ingredients in CONTRAVE. **Stop taking CONTRAVE and call your healthcare provider or go to the nearest hospital emergency room right away** if you have any of the following signs and symptoms of an allergic reaction:
  - o rash
  - o itching
  - o hives
  - o fever
  - o swollen lymph glands
  - o painful sores in your mouth or around your eyes
  - o swelling of your lips or tongue
  - o chest pain
  - o trouble breathing
- **Increases in blood pressure or heart rate.** Some people may get high blood pressure or have a higher heart rate when taking CONTRAVE. Your healthcare provider should check your blood pressure and heart rate before you start taking, and while you take CONTRAVE.
- **Liver damage or hepatitis.** One of the ingredients in CONTRAVE, naltrexone can cause liver damage or hepatitis. Stop taking CONTRAVE and tell your healthcare provider if you have any of the following symptoms of liver problems:

- stomach area pain lasting more than a few days
- dark urine
- yellowing of the whites of your eyes
- tiredness

Your healthcare provider may need to stop treating you with CONTRAVE if you get signs or symptoms of a serious liver problem.

- **Manic episodes.** One of the ingredients in CONTRAVE, bupropion can cause some people who were manic or depressed in the past to become manic or depressed again.
- **Visual problems (angle-closure glaucoma).** One of the ingredients in CONTRAVE, bupropion, can cause some people to have visual problems (angle-closure glaucoma). Signs and symptoms of angle-closure glaucoma may include:
  - eye pain
  - changes in vision
  - swelling or redness in or around the eye

  Talk with your healthcare provider to find out if you are at risk for angle-closure glaucoma and to get treatment to prevent it if you are at risk.
- **Increased risk of low blood sugar (hypoglycemia) in people with type 2 diabetes mellitus who also take medicines to treat their diabetes.** Weight loss can cause low blood sugar in people with type 2 diabetes mellitus who also take medicines used to treat type 2 diabetes mellitus (such as insulin or sulfonylureas). You should check your blood sugar before you start taking CONTRAVE and while you take CONTRAVE.

The most common side effects of CONTRAVE include:

- nausea
- constipation
- headache
- vomiting
- dizziness
- trouble sleeping
- dry mouth
- diarrhea

These are not all of the possible side effects of CONTRAVE.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store CONTRAVE?

Store CONTRAVE at room temperature between 59°F to 86°F (15°C to 30°C).

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

General information about the safe and effective use of CONTRAVE.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use CONTRAVE for a condition for which it was not prescribed. Do not give CONTRAVE to other people, even if they have the same symptoms that you have. It may harm them.

If you take a urine drug screening test, CONTRAVE may make the test result positive for amphetamines. If you tell the person giving you the drug screening test that you are taking CONTRAVE, they can do a more specific drug screening test that should not have this problem.

You can ask your pharmacist or healthcare provider for information about CONTRAVE that is written for health professionals.

What are the ingredients in CONTRAVE?

Active ingredient: naltrexone hydrochloride and bupropion hydrochloride

Inactive ingredients: microcrystalline cellulose, hydroxypropyl cellulose, lactose anhydrous, L-cysteine hydrochloride, crospovidone, magnesium stearate, hypromellose, edetate disodium, lactose monohydrate, colloidal silicon dioxide, Opadry II Blue and FD&C Blue #2 aluminum lake

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For more information, go to www.contrave.com or call 1-877-298-8340.

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