# CONTRAVE (naltrexone/bupropion)

Intended for weight loss in adults who are obese or overweight with at least one weight-related condition

## BOTTOM LINE

- **CONTRAVE's benefit is modest.** In one of the largest studies, obese and overweight people who took CONTRAVE for up to 56 weeks lost about 9 pounds more on average compared to those who took a placebo. In that study, 42 percent of people who took Contrave lost at least 5 percent of their body weight compared with 17 percent of those who took a placebo.

- **CONTRAVE's harm**

> **Black Box Warning** CONTRAVE carries the most serious level of FDA warning because it contains the antidepressant bupropion. All antidepressants carry a Black Box Warning because they **can increase suicidal thoughts and behaviors in adolescents and young adults taking antidepressants**. For every 1,000 adolescents taking antidepressants, 14 more will become suicidal than if they didn't take the medication. In young adults, those numbers are 5 in 1,000. **New or worsening depression or suicidal thoughts have also been reported in patients taking BUPROPION to help them stop smoking.**

**Serious side effects:**

- **Some people who were depressed experienced delusions, hallucinations, paranoia, and confusion.**
- **Serious eye problems** (angle-closure glaucoma).
- **When used with diabetes medications, CONTRAVE can cause low blood sugar.**
- **Severe, potentially fatal skin reactions** (blisters, peeling rash, mouth ulcers).
- **Potentially fatal liver failure.**

**Bothersome side effects:** The most common side effects include **nausea, vomiting, constipation, headache**, and **dizziness**. In the clinical trials, 24 percent of people stopped taking CONTRAVE because of side effects, compared to 12 percent who took a placebo.

**Short track record for this use means that new, unexpected side effects are possible:** The ingredients in CONTRAVE were first approved by FDA in 1984 (NALTREXONE for opioid addiction) and 1985 (BUPROPION for depression). The combination wasn't approved for weight loss until 2014 based on studies in which about 2,500 people took approved doses of the drug for up to a year. As with all drugs, important side effects may emerge when larger numbers of people with other conditions and on other medication take this new drug combination for a longer time than the time frame of the trials.

The FDA is concerned that CONTRAVE might increase the risk of heart attack or stroke, so it required the manufacturer to conduct a trial to determine if the medication is safe for the heart, but the results are not expected until 2021. So for now, it's not known if CONTRAVE increases the risk of cardiovascular problems.

# DRUGFACTSBOX™ CONTRAVE

ConsumerReports®

## Who is it approved for?

- Adults who are obese—a body mass index, or BMI, of 30 or higher. (Calculate your BMI at ConsumerReports.org/bmi)
- Adults who are overweight—a BMI of 27 to 29.9—and also have at least one weight-related health problem, such as high blood pressure, high cholesterol, heart disease, or type 2 diabetes.

## Who should NOT take it?

- People who have **high blood pressure**, a history of **seizures**, or an **eating disorder** such as anorexia (eating too little) or bulimia (eating too much).
- People who take any of the following:
  - **Opioid medications**, including oxycodone (Oxycontin) and hydrocodone combined with acetaminophen (Vicodin), as well as **opioid prescription cough and cold products**.
  - **Methadone**, **buprenorphine**, or other **medication to help stop taking opioids**.
  - **Buproprion** (Wellbutrin, Aplenzin, and generic)
  - **Monoamine oxidase inhibitors** (MAOIs) such as phenelzine (Nardil) and tranylcypromine (Parnate). **If you take an MAOI, you must stop at least 14 days before taking CONTRAVE.**
- Women who are pregnant or breastfeeding because **CONTRAVE might harm your baby**.

## Precautions

- **Make sure your doctor knows** if you have a history of **depression, bipolar disorder, or other mental illness**, or have had **suicidal thoughts** in the past. CONTRAVE can cause those problems to come back.
- **Minimize or avoid use of alcohol while taking CONTRAVE** since taking it with alcohol increases the chance of seizures. If you are a heavy drinker, do NOT stop alcohol suddenly without first talking to your doctor.
- **Never mix CONTRAVE and opioid medications** because that can cause an overdose or serious withdrawal symptoms. Because medications can linger in your system, you must **wait 7 to 10 days between taking any opioid and taking CONTRAVE**.
- Your doctor should **check your blood pressure and heart rate before you start taking CONTRAVE and routinely afterward**.
- **Call your doctor right away if you experience symptoms of:**
  - **Liver damage** including stomach pain lasting more than a few days, dark urine, yellowing of the whites of your eyes, or tiredness,
  - **Visual problems** (angle-closure glaucoma) such as eye pain, changes in vision, swelling or redness in or around the eye.
  - **Low blood sugar** such as shaking, sweating, dizziness, weakness, or feeling jittery – those symptoms are especially likely if you take other medications that lower blood sugar (such as pills or injections for diabetes).
  - **Serious allergic reaction** such a rash or hives; swelling of face, lips, tongue, or throat; or trouble breathing or swallowing. **Stop the drug**.
  - **Opioid overdose** such as trouble breathing, extreme drowsiness with slow or shallow breathing, or feeling faint, dizzy, or confused. **You or someone close to you should get emergency help**
  - **Seizures** CONTRAVE can cause **seizures**. If you have a seizure, **stop the drug**.

## What other choices are there?

- **Nondrug choices**
  Diet and exercise programs, behavior modification with a therapist, and weight-loss surgery for patients with severe obesity—BMI greater than 40.
- **Other drug choices**
  Other FDA-approved medications for weight loss, including the prescription drugs: liraglutide (SAXENDA), lorcaserin (BELVIQ), orlistat (XENICAL), and phentermine/topiramate (QSYMIA) and the over-the-counter version of orlistat (ALLI).

## Study Findings: Benefit for people with diabetes

The FDA approved CONTRAVE for weight loss in people with diabetes based on one clinical trial. It included 505 adults with diabetes who were either obese or overweight with or without a weight-related health problem. They had an average age of 54, an average weight of 230 pounds, and an average A1c of 8 points. They were given either CONTRAVE or a placebo twice daily for 1 year. Everyone was advised to exercise and eat 500 fewer calories a day. Here's what happened:

| **How did CONTRAVE help?*** | **CONTRAVE** (32 mg/360 mg) | **PLACEBO** (No drug) |
|---|---|---|
| ■ **How much weight did people lose?** | | |
| On average, CONTRAVE users lost about 5 more pounds than placebo users. | Lost 9 pounds (or about 4% of their body weight) | Lost 4 pounds (or about 2% of their body weight) |
| ■ **Blood sugar control** | | |
| On average, CONTRAVE users had better control of blood sugar (A1c 0.5 points better). | 0.6 points better | 0.1 points better |

## Study Findings: Benefit for people without diabetes

The FDA approved CONTRAVE for weight loss based on four clinical trials. People in the studies were either obese: (BMI of 30 or higher), or they were overweight (BMI of 27 to 29.9), with at least one weight-related health problem. Results were about the same in all studies. In one of the largest studies that involved 1,164 men and women without diabetes with an average age of 44, and an average weight of 220 pounds. They were given either CONTRAVE or a placebo twice daily for a year. Everyone underwent behavioral counseling and was advised to exercise and eat 500 fewer calories a day. Here's what happened:

| **How did CONTRAVE help?*** | **CONTRAVE** (32 mg/360 mg) | **PLACEBO** (No drug) |
|---|---|---|
| ■ **How much weight did people lose?** | | |
| On average, CONTRAVE users lost about 9 pounds more than placebo users. | Lost 12 pounds (or about 5% of their body weight) | Lost 3 pounds (or about 1% of their body weight) |
| ■ **How many people lost weight and how much?** | | |
| More CONTRAVE users lost between 5 and 9 percent of their body weight. | 21% | 10% |
| More CONTRAVE users lost 10 percent or more of their body weight. | 21% | 7% |

| Study Findings: Side effects for people with AND without diabetes | | |
|---|---|---|
| **What were CONTRAVE's side effects?*** | **CONTRAVE** (32 mg/360 mg) | **PLACEBO** (No drug) |
| ■ **Serious side effects** (Based on about 4,000 people in all CONTRAVE trials) | | |
| **Increased blood pressure** (0.9% more people) | 2.4% | 1.5% |
| **Faster pulse** (2 beats per minute faster) | 73 beats / minute | 71 beats / minute |
| **Worsening of kidney function** (0.5% more people) | 0.6% | 0.1% |
| **Seizures** (0.1% more people) | 0.1% | 0% |
| ■ **Bothersome side effects** (Based on about 4,000 patients in all CONTRAVE trials) | | |
| **Nausea** (26% more) | 33% | 7% |
| **Constipation** (12% more) | 19% | 7% |
| **Vomiting** (8% more) | 11% | 3% |
| **Headache** (8% more) | 18% | 10% |
| **Dizziness** (7% more) | 10% | 3% |
| **Dry mouth** (6% more) | 8% | 2% |
| **Insomnia** (3% more) | 9% | 6% |
| **Tremor** (3% more) | 4% | 1% |
| **Hot flush** (3% more) | 4% | 1% |
| **Ringing in ears** (3% more) | 3% | 1% |
| **Belly pain** (2% more) | 3% | 1% |
| **Diarrhea** (2% more) | 7% | 5% |
| **Excessive sweating** (2% more) | 3% | 1% |
| **Trouble concentrating** (2% more) | 3% | 1% |
| **Anxiety** (1% more) | 4% | 3% |
| ■ **Uncommon serious side effects seen with CONTRAVE** (or other drugs containing buproprion or nalexone) | | |
| **New or worsening depression or suicidal thoughts**, especially in people undergoing smoking cessation treatment. | | |
| **Return of mania or depression in people with a history of those disorders.** | | |
| **Low blood sugar** in people with diabetes. | | |
| **Visual problems** – angle-closure glaucoma. | | |

* This information comes from:
The FDA-approved drug label for Contrave
FDA Advisory Committee materials for CONTRAVE
Orexigen's briefing materials for CONTRAVE

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