Reduce hunger and help control cravings with CONTRAVE®

Understanding and identifying patients who are ready to start their weight-loss journey with CONTRAVE® is key to helping them reach their weight-loss goals.

This guide is designed to outline the key characteristics and weight-loss results of real-world patients who are ready for CONTRAVE.

Indication

CONTRAVE is indicated as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adults with an initial body mass index (BMI) of:

- 30 kg/m^2 or greater (obese) or
- 27 kg/m^2 or greater (overweight) in the presence of at least one weight-related comorbid condition (eg, hypertension, type 2 diabetes mellitus, or dyslipidemia)

Limitations of Use

The effect of CONTRAVE on cardiovascular morbidity and mortality has not been established. The safety and effectiveness of CONTRAVE in combination with other products intended for weight loss, including prescription drugs, over-the-counter drugs, and herbal preparations, have not been established.

Important Safety Information

WARNING: SUICIDAL THOUGHTS AND BEHAVIORS

- **Increased risk of suicidal thinking and behavior in children, adolescents, and young adults taking antidepressants for major depressive disorder and other psychiatric disorders**
  - **CONTRAVE contains bupropion, the same active ingredient as some other antidepressant medications or products for smoking cessation**
- **Monitor for worsening and emergence of suicidal thoughts and behaviors**
- **CONTRAVE has not been studied in pediatric patients**

Please see additional Important Safety Information, including complete boxed warning for suicidal thoughts and behaviors, on pages 4–5.

Contrave®
(naltrexone HCl/bupropion HCl)
8 mg/90 mg • Extended-Release Tablets

Janine wanted lasting control over what and how much she ate

Janine's starting point: July 2015	
Age	40
BMI	42.3
Lifestyle Situation	• Married with 4 teenage kids—3 daughters and 1 son • Psychiatric mental health nurse practitioner • Also currently getting her PhD in nursing education
Past Weight-Loss Experience	• Weight problems started after her second child and have been a constant struggle ever since • Tried various lifestyle changes and programs, and has also been on and off prescription treatments, including phentermine, in the past — She'd typically lose weight, then gain it back and more after stopping treatment

Janine's doctor prescribed CONTRAVE to help her make lasting behavior changes and control her cravings

7 months into taking CONTRAVE: March 2016	
Age	40
BMI	30.0
Since Starting Treatment	• Janine has lost more than 10% of her body weight • She found that CONTRAVE has helped her to lose weight by changing her eating habits and helping to control not only how much she eats, but what she eats and allowed her to stick with her diet and exercise plan • Her weight loss has increased her energy level and she is more active with her husband and kids

"I now eat to live; I don't live to eat. I feel better about my weight and the food I'm choosing is a huge part of that."

Actual patient. Results not typical. Individual results may vary.

Contraindications

CONTRAVE is contraindicated in: uncontrolled hypertension; seizure disorder or a history of seizures; use of other bupropion-containing products; bulimia or anorexia nervosa, which increase the risk for seizure; chronic opioid or opiate agonist (eg, methadone) or partial agonist (eg, buprenorphine) use, or acute opiate withdrawal; patients undergoing an abrupt discontinuation of alcohol, benzodiazepines, barbiturates, and antiepileptic drugs; use during/within 14 days following treatment with monoamine oxidase inhibitors (MAOIs), as there is an increased risk of hypertensive reactions when CONTRAVE is used concomitantly with MAOIs, including reversible MAOIs such as linezolid or intravenous methylene blue; known allergy to any component of CONTRAVE, as anaphylactoid/anaphylactic reactions and Stevens-Johnson syndrome have been reported; and pregnancy.

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Jim needed help to not only lose weight, but to keep it off as well

Jim's starting point: Early 2015	
Age	71*
BMI	33.9
Comorbid Conditions	• Hypertension† • Type 2 diabetes†
Lifestyle Situation	• Retired, but works part time as a delivery truck driver • Married with 3 grown kids
Treatments	• 3 medications to manage his hypertension • 2 oral medications to manage his type 2 diabetes
Past Weight-Loss Experience	• Was very trim until his early 30s when his weight issues started • It's been a constant struggle of weight loss and regain

Jim's doctor prescribed CONTRAVE to help support his weight-loss goals

A year into taking CONTRAVE: January 2016	
Age	72
BMI	26.4
Since Starting Treatment	• Saw improvements in his health due to weight loss, including no longer needing to take diabetes medications and a reduction in the number of medications for hypertension • He found that his weight loss made him better able to actively participate in his outdoor hobbies again • Feels like he's able to make smart choices now and maintain a more balanced diet

"Since I started on CONTRAVE, changed my diet, and started exercising more, I can actually see results! It's helped me lose weight. I've seen changes in my A1C—I'm not taking any more diabetes medication after 25 years of being on them."

*CONTRAVE should be used with caution in patients over 65 years of age.
Actual patient. Results not typical. Individual results may vary.
†CONTRAVE is not approved to treat hypertension or type 2 diabetes.

Important Safety Information

Hypoglycemia with Use of Antidiabetic Medications

Weight loss may increase the risk of hypoglycemia in patients with type 2 diabetes mellitus treated with insulin and/or insulin secretagogues (eg, sulfonylureas). Measurement of blood glucose levels prior to starting CONTRAVE and during CONTRAVE treatment is recommended in patients with type 2 diabetes. Decreases in medication doses for antidiabetic medications that are non-glucose-dependent should be considered to mitigate the risk of hypoglycemia.

Please see additional Important Safety Information, including complete boxed warning for suicidal thoughts and behaviors, on pages 4–5.

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Important Safety Information for CONTRAVE (naltrexone HCl and bupropion HCl) extended-release tablets

WARNING: SUICIDAL THOUGHTS AND BEHAVIORS

Suicidality and Antidepressant Drugs

CONTRAVE® is not approved for use in the treatment of major depressive disorder or other psychiatric disorders. CONTRAVE contains bupropion, the same active ingredient as some other antidepressant medications (including, but not limited to, WELLBUTRIN, WELLBUTRIN SR, WELLBUTRIN XL, and APLENZIN). Antidepressants increased the risk of suicidal thoughts and behavior in children, adolescents, and young adults in short-term trials. These trials did not show an increase in the risk of suicidal thoughts and behavior with antidepressant use in subjects over age 24; there was a reduction in risk with antidepressant use in subjects aged 65 and older. In patients of all ages who are started on CONTRAVE, monitor closely for worsening, and for the emergence of suicidal thoughts and behaviors. Advise families and caregivers of the need for close observation and communication with the prescriber. CONTRAVE is not approved for use in pediatric patients.

Contraindications

CONTRAVE is contraindicated in: uncontrolled hypertension; seizure disorder or a history of seizures; use of other bupropion-containing products; bulimia or anorexia nervosa, which increase the risk for seizure; chronic opioid or opiate agonist (eg, methadone) or partial agonist (eg, buprenorphine) use, or acute opiate withdrawal; patients undergoing an abrupt discontinuation of alcohol, benzodiazepines, barbiturates, and antiepileptic drugs; use during/within 14 days following treatment with monoamine oxidase inhibitors (MAOIs), as there is an increased risk of hypertensive reactions when CONTRAVE is used concomitantly with MAOIs, including reversible MAOIs such as linezolid or intravenous methylene blue; known allergy to any component of CONTRAVE, as anaphylactoid/anaphylactic reactions and Stevens-Johnson syndrome have been reported; and pregnancy.

WARNINGS AND PRECAUTIONS

Suicidal Behavior and Ideation

All patients being treated with antidepressants for any indication should be monitored and observed for clinical worsening, suicidality, and unusual changes in behavior, especially during the initial few months of a course of drug therapy, or at times of dose changes.

Families and caregivers of patients being treated with antidepressants for major depressive disorder or other indications, both psychiatric and nonpsychiatric, should be alerted about the need to monitor patients for the emergence of suicidality, anxiety, agitation, irritability, unusual changes in behavior, and other symptoms, and to report such symptoms immediately to healthcare providers.

Neuropsychiatric Adverse Events and Suicide Risk in Smoking Cessation Treatment

CONTRAVE is not approved for smoking cessation. Serious neuropsychiatric adverse events have been reported in patients taking bupropion for smoking cessation. These postmarketing reports have included changes in mood (including depression and mania), psychosis, hallucinations, paranoia, delusions, homicidal ideation, aggression, hostility, agitation, anxiety, and panic, as well as suicidal ideation, suicide attempt, and completed suicide.

Some patients who stopped smoking may have been experiencing symptoms of nicotine withdrawal, including depressed mood. Depression, rarely including suicidal ideation, has been reported in smokers undergoing a smoking cessation attempt without medication. However, some of these adverse events occurred in patients taking bupropion who continued to smoke.

Neuropsychiatric adverse events occurred in patients without and with pre-existing psychiatric disease; some patients experienced worsening of their psychiatric illnesses. Observe patients for the occurrence of neuropsychiatric adverse events. Advise patients and caregivers that the patient should stop taking CONTRAVE and contact a healthcare provider immediately if agitation, depressed mood, or changes in behavior or thinking that are not typical for the patient are observed, or if the patient develops suicidal ideation or suicidal behavior. In many postmarketing cases, resolution of symptoms after discontinuation of bupropion was reported. However, the symptoms persisted in some cases, therefore, ongoing monitoring and supportive care should be provided until symptoms resolve.

Depression, suicide, attempted suicide, and suicidal ideation have been reported in the postmarketing experience with naltrexone used in the treatment of opioid dependence. No causal relationship has been demonstrated.

Seizures

The risk of seizure is dose-related. Discontinue treatment and do not restart CONTRAVE in patients who experience a seizure. Use caution when prescribing CONTRAVE to patients with an elevated risk of seizure, including: history of head trauma or prior seizure, severe stroke, arteriovenous malformation, central nervous system tumor or infection, or metabolic disorders (eg, hypoglycemia, hyponatremia, severe hepatic impairment, and hypoxia); excessive use of alcohol or sedatives, addiction to cocaine or stimulants, or withdrawal from sedatives; patients with diabetes treated with insulin and/or oral diabetic medications (sulfonylureas and meglitinides) that may cause hypoglycemia; concomitant administration of medications that may lower the seizure threshold, including other bupropion products, antipsychotics, tricyclic antidepressants, theophylline, and systemic steroids.

Clinical experience with bupropion suggests that the risk of seizure may be minimized by adhering to the recommended dosing recommendations, including the avoidance of high-fat meals while taking CONTRAVE.

Important Safety Information for CONTRAVE, continued

Patients Receiving Opioid Analgesics

CONTRAVE should not be administered to patients receiving chronic opioids. If chronic opiate therapy is required, CONTRAVE treatment should be stopped. In patients requiring intermittent opiate treatment, CONTRAVE therapy should be temporarily discontinued and lower doses of opioids may be needed. Patients should be alerted that they may be more sensitive to opioids, even at lower doses, after CONTRAVE treatment is discontinued.

An opioid-free interval of a minimum of 7 to 10 days is recommended for patients previously dependent on short-acting opioids, and those patients transitioning from buprenorphine or methadone may need as long as two weeks. Patients should be made aware of the risks associated with precipitated withdrawal and encouraged to give an accurate account of last opioid use.

Increase in Blood Pressure (BP) and Heart Rate (HR)

CONTRAVE can cause an increase in systolic BP, diastolic BP, and/or resting HR. These events were observed in both patients with and without evidence of preexisting hypertension. In clinical practice with other bupropion-containing products, hypertension, in some cases severe and requiring acute treatment, has been reported. Blood pressure and pulse should be monitored at regular intervals.

Allergic Reactions

Anaphylactoid/anaphylactic reactions and symptoms suggestive of delayed hypersensitivity have been reported with bupropion, as well as rare spontaneous reports of erythema multiforme, Stevens-Johnson syndrome, and anaphylactic shock. Instruct patients to discontinue CONTRAVE and consult a healthcare provider if they develop an allergic or anaphylactoid/anaphylactic reaction.

Hepatotoxicity

Cases of hepatitis, clinically significant liver dysfunction, and transient asymptomatic hepatic transaminase elevations have been observed with naltrexone exposure. Warn patients of the risk of hepatic injury and advise them to discontinue CONTRAVE if they experience symptoms of acute hepatitis.

Activation of Mania

CONTRAVE treatment can precipitate a manic, mixed, or hypomanic episode. The risk appears to be increased in patients with bipolar disorder or who have risk factors for bipolar disorder. Prior to initiating CONTRAVE, screen patients for history of bipolar disorder and the presence of risk factors for bipolar disorder (eg, family history of bipolar disorder, suicide, or depression). CONTRAVE is not approved for use in treating bipolar depression.

Angle-Closure Glaucoma

The pupillary dilation that occurs following use of many antidepressant drugs, including bupropion, may trigger an angle-closure attack in a patient with anatomically narrow angles who does not have a patent iridectomy.

Hypoglycemia with Use of Antidiabetic Medications

Weight loss may increase the risk of hypoglycemia in patients with type 2 diabetes mellitus treated with insulin and/or insulin secretagogues (eg, sulfonylureas). Measurement of blood glucose levels prior to starting CONTRAVE and during CONTRAVE treatment is recommended in patients with type 2 diabetes. Decreases in medication doses for antidiabetic medications that are non-glucose-dependent should be considered to mitigate the risk of hypoglycemia.

Adverse Reactions

Most common adverse reactions (≥5%) include: nausea (32.5%), constipation (19.2%), headache (17.6%), vomiting (10.7%), dizziness (9.9%), insomnia (9.2%), dry mouth (8.1%), and diarrhea (7.1%).

Drug Interactions

Use caution when prescribing CONTRAVE concomitantly with dopaminergic drugs (levodopa and amantadine), drugs metabolized by CYP2D6, or drugs that lower the seizure threshold. Avoid concomitant use with MAOIs and CYP2B6 inducers. Reduce CONTRAVE dose when taken with CYP2B6 inhibitors. CONTRAVE can cause false positive urine test results for amphetamines.

Please see Full Prescribing Information for complete Boxed Warning and Medication Guide for CONTRAVE.

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