*Based on the number of prescription fills for brand name weight-loss drugs in the IQVIA database, July 2021 to June 2022.

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

Do your patients seeking weight loss struggle to control their cravings?

Your patients who are overweight or struggling with obesity may find it hard to control cravings that are associated with emotional eating.[1-3]

Help them **lose weight and keep it off** with CONTRAVE—an FDA-approved, nonstimulant, oral weight-loss medication designed to reduce hunger and control cravings.[1,2†]

†The exact neurochemical effects of CONTRAVE leading to weight loss are not fully understood.[1]

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.

Please see Important Safety Information throughout and the Full Prescribing Information, including Medication Guide, for CONTRAVE.

IMPORTANT SAFETY INFORMATION

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.

Not an actual patient.

Maya

Age: 35

BMI: 30 kg/m^2

Job: account executive

Lifestyle

- Works a high-pressure job with long hours and has very little personal time
- Prioritizes the needs of others at the expense of her own self-care

Medical history

- Takes a selective serotonin reuptake inhibitor (SSRI) for anxiety and depression
- Has controlled hypertension

Eating habits

- Snacks throughout the day, often when she isn't hungry
- Feels frustrated by her weight gain and powerless to control her cravings

Weight-loss history

- Has tried dieting apps and squeezes in exercise when she can but knows that these alone aren't enough to tackle her weight gain
- Recognizes that her eating habits seem tied to her emotions but has trouble bringing it up with her doctor

Patients like Maya want to lose weight, but they struggle with emotional eating and controlling the cravings that occur when they are stressed throughout the day. Adding CONTRAVE, a weight-loss medication designed to reduce hunger and control cravings, to diet and exercise may help them lose weight and keep it off.[1-3]

IMPORTANT SAFETY INFORMATION (cont'd)

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.

Please see Important Safety Information throughout and the Full Prescribing Information, including Medication Guide, for CONTRAVE.

IMPORTANT SAFETY INFORMATION (cont'd)

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. Such monitoring should include daily observation by families and caregivers. Prescriptions for CONTRAVE should be written for the smallest quantity of tablets consistent with good patient management, in order to reduce the risk of overdose.

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.

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Lifestyle

- Serves as the primary caregiver for her 3 children and structures her day around family
- Tries to walk and carve out personal time each day but daily demands often interfere

Medical history

- Has prediabetes (A1C: 5.8%)

Eating habits

- Doesn't have an established breakfast or lunch routine and relies on fast food and snacks for her meals
- Tries to eat healthy during the day but overeats in the evening once her children are asleep and the stressors of the day catch up with her

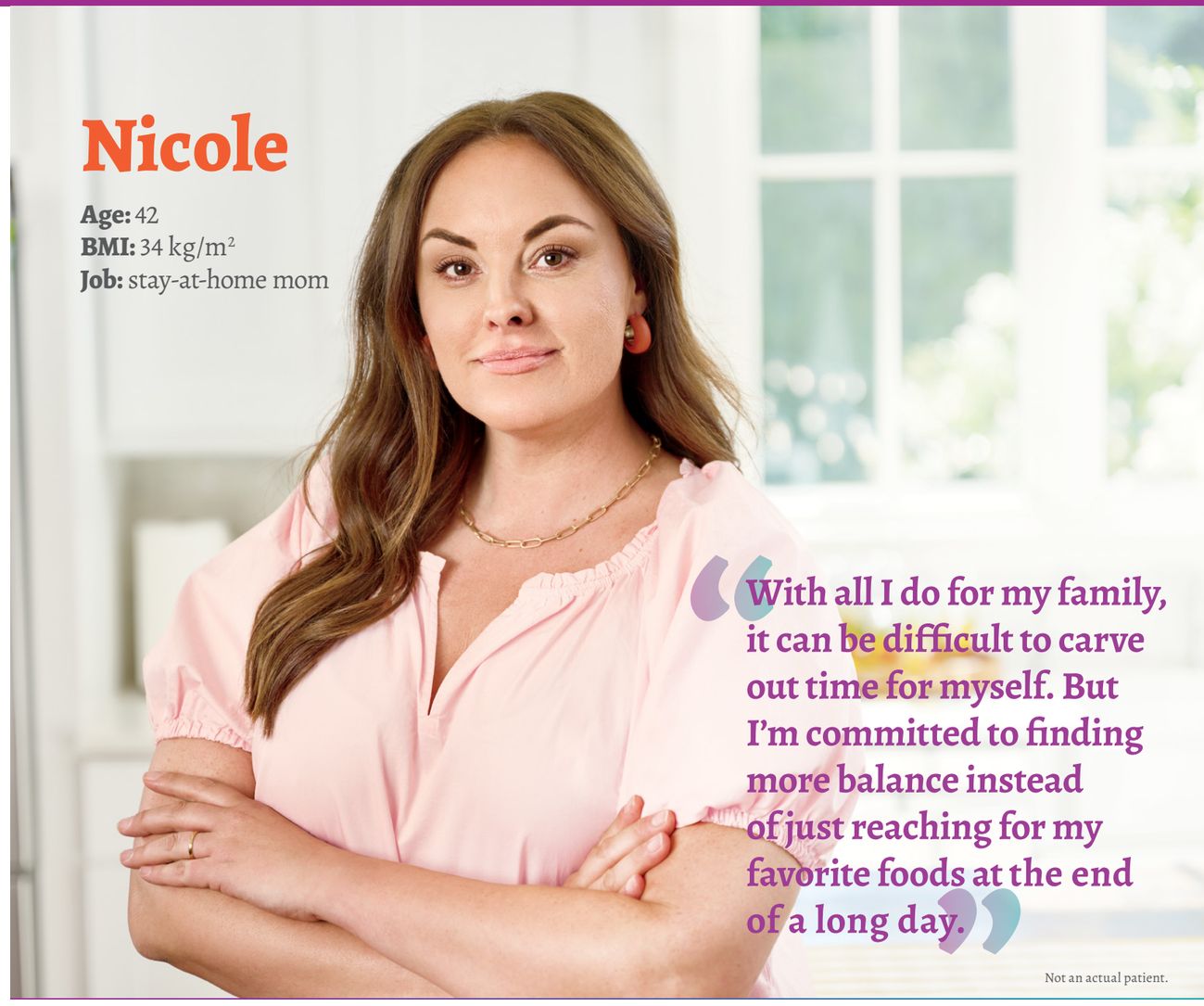
Weight-loss history

- Has had some success with weight-loss support groups but can't keep the weight off long term
- Has a fear of needles, which has made her reluctant to consider certain medications

Losing weight can be a challenge for patients like Nicole, who find it difficult to resist cravings associated with emotional eating and make their health a priority. That's why CONTRAVE, along with a reduced-calorie diet and increased physical activity, may be right for them.[1-3]

Nicole

Age: 42
BMI: 34 kg/m^2
Job: stay-at-home mom



"With all I do for my family, it can be difficult to carve out time for myself. But I'm committed to finding more balance instead of just reaching for my favorite foods at the end of a long day."

Not an actual patient.

IMPORTANT SAFETY INFORMATION (cont'd)

Seizures

Bupropion, a component of CONTRAVE, can cause 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, in particular: the total daily dose of CONTRAVE does not exceed 360 mg of the bupropion component (ie, four tablets per day); the daily dose is administered in divided doses (twice daily); the dose is escalated gradually; no more than two tablets are taken at one time; coadministration of CONTRAVE with high-fat meals is avoided; if a dose is missed, a patient should wait until the next scheduled dose to resume the regular dosing schedule.

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IMPORTANT SAFETY INFORMATION (cont'd)

Patients Receiving Opioid Analgesics

Vulnerability to Opioid Overdose: CONTRAVE should not be administered to patients receiving chronic opioids, due to the naltrexone component, which is an opioid receptor antagonist. 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 attempt by a patient to overcome any naltrexone opioid blockade by administering large amounts of exogenous opioids is especially dangerous and may lead to a fatal overdose or life-threatening opioid intoxication (e.g., respiratory arrest, circulatory collapse). Patients should be told of the serious consequences of trying to overcome the opioid blockade.

Precipitated Opioid Withdrawal: 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.

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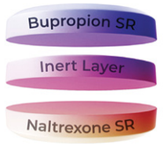
Consider CONTRAVE for your patients who struggle with emotional eating

- The **only FDA-approved 2-in-1 combination drug** containing sustained-release (SR) naltrexone and bupropion that targets the brain's appetite regulatory center and the mesolimbic reward system[1]*
- Clinically proven to help patients **lose weight and keep it off** by targeting the parts of the brain that regulate hunger and cravings[1,2]



*The exact neurochemical effects of CONTRAVE leading to weight loss are not fully understood.[1]

Visit CONTRAVEHCP.com and learn more

IMPORTANT SAFETY INFORMATION (cont'd)

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 measured prior to starting therapy with CONTRAVE and should be monitored at regular intervals consistent with usual clinical practice, particularly among patients with controlled hypertension prior to treatment.

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 (eg, skin rash, pruritus, hives, chest pain, edema, or shortness of breath) during treatment.

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 seek medical attention if they experience symptoms of acute hepatitis. Use of CONTRAVE should be discontinued in the event of symptoms and/or signs of acute hepatitis.

Activation of Mania

Bupropion, a component of CONTRAVE, is a drug used for the treatment of depression. Antidepressant 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 and consider dose reduction of drugs metabolized by CYP2D6 when using with CONTRAVE. Avoid concomitant use with MAOIs and CYP2B6 inducers. Reduce CONTRAVE dose when taken with CYP2B6 inhibitors. Dose CONTRAVE with caution when used with drugs that lower seizure threshold. Use caution and monitor for CNS toxicity when using CONTRAVE concomitantly with dopaminergic drugs (levodopa and amantadine). CONTRAVE can cause false positive urine test results for amphetamines.

Please see Important Safety Information throughout and the Full Prescribing Information, including Medication Guide, for CONTRAVE.

References: 1. CONTRAVE (naltrexone HCl and bupropion HCl) [prescribing information]. Brentwood, TN: Currax Pharmaceuticals LLC; 2021. **2.** Greenway FL. Physiological adaptations to weight loss and factors favouring weight regain. *Int J Obes (Lond)*. 2015;39(8):1188-1196. doi:10.1038/ijo.2015.59 **3.** Acosta A, Camilleri M, Dayyeh BA, et al. Selection of antiobesity medications based on phenotypes enhances weight loss: a pragmatic trial in an obesity clinic. *Obesity (Silver Spring)*. 2021;29(4):662-671. doi:10.1002/oby.23120

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