RonanRx
PERSONALIZED MEDICINE

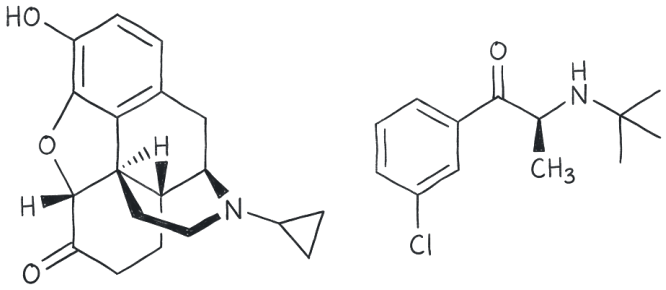
CLINICAL MONOGRAPH · METABOLIC & WEIGHT

Naltrexone-Bupropion Combination

Compounded alternative to FDA-approved Contrave

Naltrexone-bupropion is a prescription weight-loss pill. The brand-name version is Contrave, the FDA approved it in 2014. RonanRx can also make a custom-compounded version when the brand pill isn't right for you (an allergy to an ingredient, a different dose, or it's out of stock).

It works by quieting hunger and food cravings [fda_label_contrave]. The two ingredients team up: one nudges the brain's appetite controls, the other keeps that effect from wearing off too fast. Used alongside diet and exercise, most people lose 4, 5% of their body weight over a year [greenway2010].



EVIDENCE POSTURE FDA APPROVED | WELL STUDIED

REVIEWED **2026-05-08**

State-licensed 503A | Pharmacist reviewed | Doctor led | Cold-chain ready | Patient choice preserved

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FOR CLINICIANS

Naltrexone HCl 8 mg / bupropion HCl 90 mg sustained-release combination, FDA-approved as Contrave (Sept 2014) for chronic weight management in adults with BMI ≥30, or ≥27 with weight-related comorbidity, as adjunct to reduced-calorie diet and increased physical activity [fda_label_contrave; greenway2009; wadden2011]. Mechanism: bupropion stimulates POMC neurons in the arcuate nucleus via norepinephrine-dopamine reuptake inhibition; naltrexone removes beta-endorphin autoinhibitory feedback on those same neurons [hollander2013].

Phase III evidence (COR-I, COR-II, COR-BMOD, COR-Diabetes; N>4,500 combined) demonstrated approximately 4, 5% placebo-adjusted weight loss at 56 weeks; the BMOD-paired arm reached 9.3% absolute [greenway2010; apovian2013]. Label carries Boxed Warning for suicidal thoughts and behaviors; contraindicated in seizure disorder, eating disorders, chronic opioid use, uncontrolled hypertension, MAO inhibitor use, and pregnancy. Cardiovascular outcomes qualified, the LIGHT trial was terminated early without demonstrating CV benefit or excluding harm. Compounded preparations dispensed only with documented patient-specific clinical reason that manufactured Contrave cannot meet (essentially-a-copy criterion) [nissen2016; fda_essentially_a_copy].

Why Personalized Naltrexone-Bupropion Combination

Contrave's fixed 8 mg naltrexone / 90 mg bupropion sustained-release tablet was titrated up to four tablets a day in the COR program because that ratio was tractable to manufacture and tolerable across the average phase III enrollee. It was not chosen for the patient who got craving suppression from low-dose naltrexone at 3 or 4.5 mg and wants that anchored to a bupropion dose, the patient already stabilized on bupropion 150 or 300 mg for depression who needs naltrexone added without doubling their bupropion exposure, the patient whose seizure-threshold history makes 360 mg of bupropion a day a non-starter, or the patient sensitive to the lactose, microcrystalline cellulose, or FD&C dyes in the branded tablet. The fixed ratio also fails the patient who simply cannot get Contrave because of a manufactured-product backorder.

Compounding decouples the two molecules. A prescriber who knows the chart can ask for 4.5 mg naltrexone with 75 mg bupropion, or 25 mg naltrexone with 150 mg bupropion, or a naltrexone-forward ratio when craving is the dominant target and the bupropion is doing supporting work. The actives are the same naltrexone HCl and bupropion HCl the FDA reviewed in their respective monographs. What changes is the strengths, the excipients, the capsule format, and the ability to fill when Contrave is unavailable. None of that is possible inside a fixed-dose commercial tablet.

This is the older arrangement. A prescriber writes for a named patient, a pharmacist compounds it, the label carries that patient's name. Modern state licensure, USP-compliant facilities, and recall infrastructure keep it honest.

Quick Facts About Naltrexone-Bupropion Combination

Category: Combination weight-management therapy

Active ingredients: Naltrexone HCl (opioid receptor antagonist) + bupropion HCl (norepinephrine-dopamine reuptake inhibitor)

FDA-approved branded form: Contrave (naltrexone HCl 8 mg / bupropion HCl 90 mg sustained-release tablet); FDA-approved September 2014 for chronic weight management

Routes studied in humans: Oral (sustained-release tablet for the manufactured product; compounded oral capsules where dispensed)

Evidence posture: Pivotal phase III evidence (COR-I, COR-II, COR-BMOD, COR-Diabetes) supports manufactured Contrave; the compounded preparation has no separate efficacy program

FDA-approval status: Manufactured Contrave is FDA-approved for chronic weight management as adjunct to reduced-calorie diet and increased physical activity. Compounded variants are not FDA-approved.

Compounded under: 503A, patient-specific prescription only, where the manufactured FDA-approved product is not clinically appropriate

Important compounding caution: Per FDA guidance, compounded versions of an FDA-approved drug are generally permissible only when the manufactured product cannot meet the patient's medical need (e.g., excipient sensitivity, dose individualization, manufactured-product unavailability). Routine compounding of essentially-a-copy preparations is restricted.

SPECIALS: PATIENT-SPECIFIC PRESCRIPTION ONLY

Naltrexone-Bupropion Combination described in this monograph is a 503A compounded preparation. Every dose is made on a prescription, for a named patient, by a licensed pharmacist. It is not a stocked, mass-manufactured product.

- **Made to order, not off a shelf.** No batch sits in a warehouse waiting for buyers. Your prescription triggers the prep.
- **Named-patient label.** The bottle carries one patient's name. The batch records carry one prescription.
- **Dose, strength, and route chosen for the patient.** A prescriber decides what gets compounded, not a manufacturer who set the strength for a trial population.
- **Licensed pharmacist on the hook.** A real person, with a license that can be pulled, signs off on every prep. State inspectors check the facility.
- **Compounded drugs are not FDA-approved.** They should not be evaluated using branded-drug trial data alone. Availability varies by state and prescribed medication.

How This Differs from a Research-Use-Only Website

A research-use-only website ships a vial from a warehouse. There is no prescription, no pharmacist, no facility inspection, and no way to recall the product if something is wrong with it. If the vial is mislabeled, contaminated, or under-potent, there is nobody whose license is at stake.

A 503A compounding pharmacy is the other thing. The doctor writes the prescription. A licensed pharmacist, whose name is on the label, prepares the medicine in a facility the state inspects. If something goes wrong, there is a person and a license on the hook, and a documented chain of custody on every lot. That accountability is what makes it safe.

What is Naltrexone-Bupropion Combination?

Naltrexone-bupropion is a combination of two long-established active ingredients with different individual indications, formulated together for chronic weight management. Bupropion HCl (originally introduced for major depressive disorder in 1985 and later for smoking cessation) is a norepinephrine-dopamine reuptake inhibitor. Naltrexone HCl (introduced 1984) is a competitive antagonist at mu- and kappa-opioid receptors used in opioid-use and alcohol-use disorders.

The combination was developed on the rationale that naltrexone removes a beta-endorphin-mediated negative feedback signal that otherwise limits bupropion's effect on hypothalamic POMC neurons [fda_label_contrave]. This was demonstrated preclinically by Greenway and colleagues and supported the design of the phase III COR program in human obesity [greenway2009].

The resulting branded product, Contrave, was FDA-approved in September 2014 as an adjunct to lifestyle modification in adults with body mass index ≥30 kg/m² (obesity) or ≥27 kg/m² with at least one weight-related comorbidity such as hypertension, type 2 diabetes, or dyslipidemia.

How Naltrexone-Bupropion Combination Works

Bupropion stimulates POMC (pro-opiomelanocortin) neurons in the hypothalamic arcuate nucleus through inhibition of norepinephrine and dopamine reuptake. POMC neurons release α-MSH, which activates MC4 receptors that drive satiety and reduced food intake. Bupropion alone produces modest weight reduction, but its effect is self-limiting because POMC neurons co-release beta-endorphin that feeds back through mu-opioid receptors on the same neurons to inhibit further firing.

Naltrexone blocks that beta-endorphin autoinhibitory loop by antagonizing mu-opioid receptors on POMC neurons. With the brake removed, bupropion's stimulatory effect on POMC neurons is sustained and amplified, yielding greater weight loss in combination than either drug alone [billes2008; wadden2011].

Beyond appetite, the combination also engages mesolimbic reward circuits implicated in food craving [greenway2009]. Reduction in hedonic eating and craving has been observed in functional imaging and behavioral measures from the COR-BMOD subset analyses.

Biological Role of Naltrexone-Bupropion Combination

The naltrexone-bupropion combination acts on two endogenous regulatory systems that govern appetite, food reward, and energy balance: the central catecholamine pathways (norepinephrine and dopamine) that drive POMC neuron activity in the hypothalamic arcuate nucleus, and the endogenous opioid system whose mu-opioid receptors normally provide feedback inhibition on those same neurons [billes2008].

POMC (pro-opiomelanocortin) is a precursor protein cleaved into multiple bioactive peptides including α-MSH (which activates MC4 receptors and suppresses appetite) and beta-endorphin (which acts on mu-opioid receptors). Beta-endorphin co-released from POMC neurons binds mu-opioid receptors on those neurons in an autoinhibitory loop. Naltrexone, a competitive mu-opioid antagonist with a long history of use in opioid- and alcohol-use disorders, blocks that autoinhibition.

Bupropion, originally introduced as an antidepressant and later for smoking cessation, increases synaptic norepinephrine and dopamine availability via reuptake inhibition [stahl2004]. In the arcuate nucleus this stimulates POMC firing. The combination therefore engages both an excitatory drive (bupropion) and disinhibition (naltrexone) on the same satiety-driving neurons, producing a sustained increase in α-MSH release and reduced food intake that exceeds either drug's individual effect [greenway2009; yeomans1997; volpicelli1992].

Detailed Mechanism of Naltrexone-Bupropion Combination

POMC neurons in the hypothalamic arcuate nucleus integrate peripheral metabolic signals (leptin, insulin, ghrelin) and project to second-order neurons in the paraventricular nucleus that govern food intake. Activation of POMC neurons cleaves α-MSH from the POMC precursor, which binds MC4 receptors to suppress appetite. POMC neurons also co-release beta-endorphin, which binds mu-opioid receptors on the same neurons in an autoinhibitory feedback loop that limits sustained firing, the mechanistic vulnerability that the naltrexone-bupropion combination was designed to exploit [greenway2009].

Bupropion, through inhibition of norepinephrine and dopamine reuptake, increases monoamine availability in the arcuate, depolarizing POMC neurons and increasing α-MSH release. The dual NE/DA reuptake-inhibition mechanism of bupropion was characterized comprehensively by Stahl and colleagues across both the depression and weight-management literatures [stahl2004]; weight-loss-specific catecholamine effects in preclinical models were dissected by Billes and Cowley [billes2008]. Beyond the hypothalamus, bupropion's dopaminergic action engages mesolimbic reward circuits that govern food

palatability, circuits independently implicated in human obesity by Wang, Volkow and colleagues, who reported reduced striatal dopamine D2-receptor availability in patients with obesity [wang2001].

Naltrexone, a competitive mu-opioid antagonist, blocks beta-endorphin's autoinhibitory effect on POMC neurons. The opioid system's role in food reward and palatability had already been established by Yeomans and colleagues, who showed that naltrexone alone reduces palatability-driven food intake in humans [yeomans1997]. The combination produces a sustained increase in POMC firing and α-MSH output that exceeds either drug's individual effect. This was demonstrated in a human phase 2 RCT in which combined bupropion + naltrexone produced greater weight loss than either monotherapy or placebo [greenway2009_phase2]. Functional MRI work by Wang and colleagues showed that 4 weeks of combined naltrexone-bupropion altered resting-state functional connectivity in the hypothalamus and reward-circuit regions in ways consistent with reduced food-cue reactivity [wang2018_fmri].

Naltrexone's parent compound has a relatively short plasma half-life (~4 h), but its active metabolite 6β-naltrexol has a longer half-life (~13 h) and contributes meaningfully to sustained mu-opioid receptor occupancy across the dosing interval, a PK property characterized in the foundational Verebey work [verebey1976]. Bupropion's metabolism by CYP2B6 to hydroxybupropion and other active metabolites was mapped by Hsyu and colleagues [hsyu1997], and explains both the prolonged effective half-life (~21 h with metabolites) and the substantial cytochrome-mediated drug-interaction profile that shapes the combination's labeling.

Naltrexone-Bupropion Combination Research History

Bupropion's anti-obesity effect as monotherapy was characterized in the late 1990s and early 2000s, with Anderson and colleagues (2002) reporting modest but sustained weight reduction in a 48-week placebo-controlled trial [anderson2002]. The bupropion sustained-release formulation later combined with naltrexone had been validated in the smoking-cessation pivotal trial [hurt1997], and bupropion's pharmacokinetic disposition was characterized by Hsyu and colleagues in 1997 [hsyu1997]. Concurrently, naltrexone's PK profile (parent half-life ~4 h, 6β-naltrexol metabolite ~13 h) had been mapped by Verebey and colleagues a decade earlier [verebey1976], and naltrexone monotherapy at moderate doses had been examined for obesity in the 1980s with limited individual benefit but documented effects on food intake and palatability [yeomans1997]. Naltrexone's foundational efficacy in alcohol-use disorder [volpicelli1992] had established the molecule's clinical activity at mu-opioid receptors and informed dose selection for the combination. Parallel work by Wang, Volkow and colleagues had implicated striatal dopamine D2-receptor availability and mesolimbic reward circuits in human obesity [wang2001], framing the reward-circuit rationale for engaging both catecholamine and opioid systems together [heymsfield2017].

Greenway and colleagues published the rational-design rationale for combining the two in 2009 [greenway2009], articulating the POMC autoinhibition hypothesis built on preclinical catecholamine-reuptake data [billes2008]. A phase 2 RCT comparing combined bupropion + naltrexone to monotherapy

and placebo, also led by Greenway, confirmed the combination's superiority over either component alone before pivotal trials began [greenway2009_phase2]. The phase III clinical development program, COR-I [greenway2010], COR-II [apovian2013], COR-BMOD [wadden2011], and COR-Diabetes [hollander2013], followed across 2010, 2013, demonstrating consistent placebo-adjusted weight loss of approximately 4, 5% in the combined-therapy arms [yanovski2014].

After the LIGHT cardiovascular outcomes trial was terminated early in 2013 over disclosure controversy, post-hoc analyses through 2016 [nissen2016] did not establish a cardiovascular benefit and did not exclude harm. Contrave's FDA approval in September 2014 was conditional on a continuing post-marketing cardiovascular outcomes commitment. Independent reviews from Caixàs [caixas2014], Sherman [sherman2016], Apovian [apovian2016], Tek [tek2016], and Velazquez & Apovian [velazquez2018] consolidated the efficacy/safety package. Functional imaging by Wang and colleagues subsequently demonstrated that combined naltrexone-bupropion modulated brain functional connectivity in regions implicated in food reward, providing in-vivo human evidence consistent with the rational-design hypothesis [wang2018_fmri]. Systematic and network meta-analyses from Khera [khera2016], Singh [singh2020], and Onakpoya [onakpoya2020] placed the combination mid-pack among approved obesity pharmacotherapies; major society guidelines from the Endocrine Society [apovian2015_guideline] and AACE [garvey2016_aace] incorporated naltrexone-bupropion into recommended pharmacotherapy algorithms [heymsfield2017; yanovski2014]. Long-term real-world evidence remains limited, though Ard and colleagues (2024) reported 12-month telehealth-cohort outcomes for FDA-approved anti-obesity medications including the combination [ard2024_realworld].

Naltrexone-Bupropion Combination Timeline

1976 • Verebey et al [verebey1976]. characterize naltrexone pharmacokinetics (parent t½ ~4 h, 6β-naltrexol metabolite t½ ~13 h), foundational PK still cited in modern labeling

1984 • Naltrexone HCl receives FDA approval for opioid use disorder

1985 • Bupropion HCl receives FDA approval for major depressive disorder

1989 • Davidson reports elevated seizure rate with original immediate-release bupropion at higher doses; FDA tightens dose ceilings [davidson1989]

1992 • Volpicelli et al [volpicelli1992]. demonstrate naltrexone efficacy in alcohol dependence, establishes mu-opioid antagonism as a clinical lever for reward-related behavior

1996 • Bupropion HCl approved for smoking cessation as Zyban; sustained-release (SR) and extended-release (XL) formulations follow

- **1997** • Hurt et al [hurt1997]. publish New England Journal of Medicine pivotal trial of sustained-release bupropion for smoking cessation
- **1997** • Hsyu et al [hsyu1997]. characterize bupropion pharmacokinetics and metabolite profile (hydroxybupropion, threohydrobupropion, erythrohydrobupropion) via CYP2B6, establishes the drug-interaction footprint carried into Contrave labeling
- **1997** • Yeomans & Gray characterize naltrexone's effect on food intake and palatability in humans, linking endogenous opioid tone to appetite [yeomans1997]
- **2001** • Wang & Volkow et al [wang2001]. (Lancet) report inverse correlation between striatal dopamine D2-receptor availability and BMI in severe obesity, frames dopaminergic reward-circuit basis for catecholamine-targeted obesity pharmacotherapy
- **2002** • Anderson et al [anderson2002]. publish 48-week placebo-controlled trial showing bupropion-induced weight loss in obesity
- **2002** • Pesola & Avasarala emergency-department case-series review reaffirms bupropion's disproportionate contribution to drug-related new-onset generalized seizures, supports the dose ceiling carried into Contrave [pesola2002]
- **2004** • Stahl et al [stahl2004]. publish comprehensive review of bupropion's dual norepinephrine-dopamine reuptake inhibition mechanism
- **2008** • Billes & Cowley demonstrate the catecholamine reuptake inhibition mechanism of weight loss in preclinical models [billes2008]
- **2009** • Greenway et al [greenway2009]. publish the rational-design rationale for combining naltrexone with bupropion based on the POMC autoinhibition hypothesis
- **2009** • Greenway et al [greenway2009_phase2]. (J Clin Endocrinol Metab) publish phase 2 RCT showing combined bupropion + naltrexone superior to either monotherapy or placebo over 24 weeks, selects doses for COR phase III
- **2010** • COR-I phase III trial published (Greenway et al., Lancet) [greenway2010]
- **2011** • COR-BMOD phase III trial published (Wadden et al.) [wadden2011]
- **2013** • COR-II and COR-Diabetes phase III trials published (Apovian et al.; Hollander et al.) [apovian2013; hollander2013]
- **2014** • FDA approves naltrexone-bupropion as Contrave for chronic weight management [fda_label_contrave]

2014 • Caixàs et al [caixas2014]. publish a clinical review of naltrexone SR/bupropion SR data through approval

2014 • Yanovski & Yanovski (JAMA) publish systematic review of long-term obesity pharmacotherapy contextualizing naltrexone-bupropion alongside orlistat, phentermine-topiramate, and lorcaserin [yanovski2014]

2015 • Endocrine Society clinical practice guideline (Apovian et al., J Clin Endocrinol Metab) incorporates naltrexone-bupropion among recommended chronic-weight-management pharmacotherapies [apovian2015_guideline]

2015 • EMA grants marketing authorization for the combination as Mysimba in the European Union

2016 • Nissen et al [nissen2016]. publish JAMA analysis of the LIGHT cardiovascular outcomes trial (terminated early); CV benefit not established

2016 • Khera et al [khera2016]. publish JAMA network meta-analysis of pharmacological treatments for obesity

2016 • AACE/ACE comprehensive clinical practice guidelines for medical care of patients with obesity (Garvey et al., Endocr Pract) include naltrexone-bupropion in recommended pharmacotherapy options [garvey2016_aace]

2016 • Sherman et al., Apovian, and Tek publish post-approval clinical reviews summarizing efficacy, safety, and patient-selection considerations [sherman2016; apovian2016; tek2016]

2017 • Heymsfield & Wadden (NEJM) review mechanisms, pathophysiology, and management of obesity, placing naltrexone-bupropion within the broader pharmacotherapy landscape [heymsfield2017]

2018 • Wang et al [wang2018_fmri]. publish first fMRI evidence that combined naltrexone-bupropion alters resting-state functional connectivity in hypothalamus and reward-circuit regions, in-vivo human confirmation of the rational-design hypothesis

2018 • Velazquez & Apovian publish updated review of pharmacological management of obesity [velazquez2018]

2020 • Singh et al [singh2020]. and Onakpoya et al [onakpoya2020]. publish systematic reviews/meta-analyses (the latter incorporating unpublished clinical study reports) confirming COR-program effect sizes and adverse-event patterns

2024 • Ard et al [ard2024_realworld]. (Obesity) publish 12-month real-world telehealth-cohort outcomes for FDA-approved anti-obesity medications including naltrexone-bupropion

2018 • Currax Pharmaceuticals acquires Contrave from Orexigen Therapeutics (chapter 11 reorganization)

Clinical Contexts for Naltrexone-Bupropion Combination

Chronic weight management in adults with obesity (BMI ≥30 kg/m²) FDA APPROVED

FDA-approved indication for the manufactured combination.

Contrave is FDA-approved as an adjunct to reduced-calorie diet and increased physical activity in adults with BMI ≥30 kg/m² [fda_label_contrave]. COR-I [greenway2010] reported approximately 6.1% placebo-adjusted weight loss at 56 weeks in the highest-dose arm. Approximately 48% of completers in the combined-therapy arm achieved ≥5% weight loss vs 16% on placebo.

Branded product: Contrave (naltrexone HCl 8 mg / bupropion HCl 90 mg ER tablet, Currax Pharmaceuticals, formerly Orexigen)

Chronic weight management in adults with overweight (BMI ≥27 kg/m²) plus weight-related comorbidity FDA APPROVED

FDA-approved indication for the manufactured combination.

Same FDA-approved indication extends to BMI ≥27 with at least one weight-related comorbidity (hypertension, type 2 diabetes, or dyslipidemia). COR-II [apovian2013] replicated the COR-I efficacy signal in a similar adult population over 56 weeks [fda_label_contrave].

Branded product: Contrave

Weight management in patients with type 2 diabetes WELL STUDIED

Studied in a dedicated phase III trial; included in the FDA label population.

COR-Diabetes [hollander2013] randomized 505 overweight or obese patients with type 2 diabetes to combined therapy or placebo over 56 weeks. Mean weight loss was 5.0% with combined therapy vs 1.8% on placebo, and HbA1c reduction averaged 0.6% vs 0.1%, supporting metabolic benefit beyond weight loss alone.

Weight management as adjunct to intensive behavior modification WELL STUDIED

Evaluated in a dedicated phase III trial; consistent with FDA-label adjunctive framing.

COR-BMOD [wadden2011] randomized participants enrolled in a 56-week intensive behavior-modification program to combined therapy or placebo. The combined-therapy arm achieved approximately 9.3% mean weight loss vs 5.1% with placebo, indicating additive benefit beyond behavioral intervention.

FDA-Approved Uses of Naltrexone-Bupropion Combination

Brand	Indication	Year	Route
Contrave	Chronic weight management in adults (BMI ≥30, or ≥27 with weight-related comorbidity) as adjunct to reduced-calorie diet and increased physical activity	2014	Oral, sustained-release tablet

The FDA-approved branded form is Contrave (naltrexone HCl 8 mg / bupropion HCl 90 mg sustained-release tablet), approved September 10, 2014 [fda_label_contrave]. Approval was based on the COR phase III program (COR-I, COR-II, COR-BMOD, COR-Diabetes), which demonstrated 4, 5% placebo-adjusted weight reduction in adults with obesity or overweight-plus-comorbidity.

The label includes a Boxed Warning regarding suicidal thoughts and behaviors associated with bupropion-containing products, and contraindications including uncontrolled hypertension, seizure disorder, eating disorders, chronic opioid use, and pregnancy. Cardiovascular safety is qualified, the LIGHT outcomes trial was terminated early and did not establish a CV benefit [nissen2016].

Compounded Naltrexone-Bupropion Combination (503A)

Compounded naltrexone-bupropion is dispensed under 503A only when the prescribing clinician documents a patient-specific need that the manufactured Contrave product cannot meet. Common documented needs include excipient sensitivity (the manufactured tablet contains specific dyes, lactose, and microcrystalline cellulose), dose individualization outside the fixed 8/90 mg ratio (for example, separate titration of components for a patient who tolerates one but not the other), or a confirmed supply interruption of the manufactured product.

Per FDA guidance for industry on compounding under 503A, a compound that is essentially a copy of a commercially available drug is generally restricted unless a prescriber has determined a clinical difference for the identified patient [fda_essentially_a_copy; fda503a]. RonanRx's pharmacist review evaluates each prescription against this criterion before dispensing and does not fill prescriptions for compounded naltrexone-bupropion that read as routine substitution for Contrave.

Compounded variants are typically dispensed as oral capsules with custom strengths matched to the patient's clinical profile. The manufactured tablet's sustained-release matrix cannot be replicated identically in compounded capsules; clinicians and patients should understand that PK/PD profiles of a compounded preparation may differ from Contrave's published characteristics.

Naltrexone-Bupropion Combination Formulations and Routes

Form	Concentration	Description
Oral capsule (compounded combination)	Custom (commonly naltrexone 4, 8 mg + bupropion 45, 90 mg per capsule)	Two-component capsule prepared under USP <795> non-sterile compounding standards. Dose individualized by the prescribing clinician; not bioequivalent to Contrave's sustained-release manufactured tablet.
Oral capsule (separated components, twice-daily)	Custom strengths per component	When a patient requires asymmetric titration of one component, naltrexone and bupropion may be dispensed as separate compounded capsules so doses can be titrated independently.

Routes used in published literature: oral.

Naltrexone-Bupropion Combination Dosing

Route	Population	Range	Duration	Study type
Oral	Adults with obesity or overweight + comorbidity (FDA-label population)	Titration over 4 weeks: week 1, naltrexone 8 mg + bupropion 90 mg every morning; week 2, twice daily; week 3, two tablets AM + one tablet PM; week 4+, two tablets twice daily (target 32 mg / 360 mg per day)	Indefinite while clinically beneficial; reassess at 16 weeks per FDA-label criterion (discontinue if <5% weight loss from baseline)	FDA-approved labeled regimen; mirrored by compounded preparations unless prescriber documents patient-specific reason for variance
Oral	Adults with renal impairment (moderate to severe; eGFR <60)	Reduced maintenance: 1 tablet (8/90 mg) AM and PM (16 mg / 180 mg per day); not recommended in end-stage renal disease	Indefinite while clinically beneficial	FDA-label population-specific guidance
Oral	Adults with hepatic impairment	Reduced maintenance: 1 tablet (8/90 mg) every morning only (8 mg / 90 mg per day); not recommended in severe hepatic impairment	Indefinite while clinically beneficial	FDA-label population-specific guidance
Oral				

Route	Population	Range	Duration	Study type
	Adults concomitantly taking strong CYP2B6 inhibitors	Maximum daily dose limited to 1 tablet AM + 1 tablet PM (16 mg / 180 mg per day) due to elevated bupropion exposure	While concomitant therapy continues	FDA-label drug-interaction guidance
Oral (bupropion monotherapy reference)	Adults, bupropion as antidepressant or smoking-cessation precedent	Bupropion HCl SR 150 mg twice daily for major depressive disorder; XL 150, 300 mg once daily; smoking cessation 150 mg BID; doses above 450 mg/day carry markedly increased seizure risk	Per indication	Approved labeling for bupropion components; informs the bupropion ceiling in combination therapy
Oral (naltrexone monotherapy reference)	Adults, naltrexone in opioid-use and alcohol-use disorders	Naltrexone HCl 50 mg orally once daily for alcohol dependence (Volpicelli regimen); 380 mg long-acting injection monthly for opioid use disorder	Per indication; alcohol dependence often 12+ weeks	Long-established labeled regimens that pre-date the obesity combination; component safety database

Doctor-prescribed and titrated. The Contrave label-defined four-week escalation balances tolerability (especially nausea, headache, insomnia) against time-to-target. Most adverse-event-driven discontinuations in the COR trials occurred during the first 4, 8 weeks; titration pacing is the primary tolerability lever.

Compounded preparations should not exceed the FDA-label maximum daily dose of naltrexone 32 mg + bupropion 360 mg in routine prescribing [fda_label_contrave]. Higher doses of either component carry component-specific risks (bupropion seizure risk above 450 mg/day; naltrexone hepatotoxicity at very high chronic doses) and have not been studied in combination.

Naltrexone-Bupropion Combination Safety

Naltrexone-bupropion safety reflects the safety profiles of both components plus a small number of combination-specific signals [1]. The most common adverse events in the COR program were nausea, constipation, headache, vomiting, dizziness, insomnia, dry mouth, and diarrhea, the majority of which were mild to moderate and concentrated in the titration period. Independent reviews summarize the same tolerability pattern, and Onakpoya and colleagues' analysis of unpublished clinical study reports [30] reproduces the published adverse-event profile [24].

The Contrave label [9] carries a Boxed Warning regarding suicidal thoughts and behaviors, derived from class-wide bupropion-containing antidepressant labeling. Bupropion also lowers seizure threshold, Davidson's 1989 review of bupropion seizure risk [17] drove the dose ceiling that the combination still observes, and Pesola & Avasarala's ED case-series review [26] reaffirmed bupropion's disproportionate contribution to drug-related new-onset generalized seizures [12]. Naltrexone-bupropion is contraindicated in patients with seizure disorder, bulimia or anorexia nervosa, chronic opioid use, abrupt discontinuation of alcohol or sedatives, and uncontrolled hypertension [1329 36].

Cardiovascular safety remains qualified. The LIGHT outcomes trial [5] was terminated early; published interim data did not demonstrate a cardiovascular benefit and did not exclude harm. A continuing post-marketing cardiovascular safety commitment was a condition of approval. Major society guidelines [32 33] reflect this qualification when recommending the combination among chronic-weight-management options [3].

Contraindications

Naltrexone-bupropion is contraindicated in: uncontrolled hypertension; seizure disorder or history of seizures; current or past bulimia nervosa or anorexia nervosa; chronic opioid use, opioid agonist use (e.g., methadone), or acute opioid withdrawal; abrupt discontinuation of alcohol, benzodiazepines, barbiturates, or antiepileptic drugs; concomitant use of MAO inhibitors (within 14 days); known allergy to bupropion or naltrexone; and pregnancy [9].

Drug interactions

Bupropion is a strong CYP2D6 inhibitor; concomitant use with CYP2D6 substrates (many antidepressants, antipsychotics, beta-blockers, and Type 1C antiarrhythmics) can raise plasma levels of those substrates substantially. Dose reductions of CYP2D6 substrates may be required [9].

Bupropion is metabolized primarily by CYP2B6; strong CYP2B6 inducers (e.g., ritonavir, efavirenz, carbamazepine) can decrease bupropion exposure, while CYP2B6 inhibitors (e.g., ticlopidine, clopidogrel) can increase it [24 9]. The maximum daily dose of the combination is reduced by half in patients on concomitant strong CYP2B6 inhibitors.

Naltrexone blocks the analgesic effect of opioid medications. Patients requiring acute opioid analgesia (postoperative, trauma) should not be on naltrexone-bupropion; naltrexone should be discontinued in advance per surgical-clearance protocols [9 25].

Adverse events

Across the COR phase III program (combined N >4,500), the most common adverse events with combined therapy vs placebo were nausea (32% vs 7%), constipation (19% vs 7%), headache (18% vs 11%), vomiting (11% vs 3%), dizziness (10% vs 3%), insomnia (9% vs 6%), and dry mouth (8% vs 2%) [1]. Adverse-event-driven discontinuation rates ranged from approximately 24, 28% with combined therapy across the four

trials, vs 12, 14% with placebo [34]. Onakpoya and colleagues' independent analysis of clinical study reports reproduces these adverse-event frequencies [30].

Serious adverse events were uncommon. Seizure rates in the combined COR development program were approximately 0.06% in the active arm, consistent with bupropion's labeled seizure risk [1726] and lower than older immediate-release bupropion formulations [2]. Reported suicidal-ideation rates did not differ statistically from placebo in the combined COR program but the Boxed Warning is class-wide [9]. Real-world tolerability and discontinuation patterns under telehealth-driven prescribing have been documented at 12 months by Ard and colleagues [37].

Monitoring Naltrexone-Bupropion Combination Therapy

Baseline assessment should include blood pressure, heart rate, complete medication review focused on opioid use and CYP2D6/CYP2B6 substrates, screening for seizure history and eating disorders, and a structured suicidal-ideation screen consistent with bupropion-containing-product labeling.

On therapy: blood pressure and heart rate at the next clinical visit and periodically thereafter; reassessment of weight loss at 16 weeks (label criterion: discontinue if <5% weight loss from baseline at 16 weeks); ongoing monitoring for mood changes, sleep disturbance, and tolerability [fda_label_contrave].

Naltrexone-Bupropion Combination Evidence Quality

Evidence supporting the manufactured Contrave is strong: a phase 2 dose-finding RCT [greenway2009_phase2] followed by four phase III randomized double-blind placebo-controlled trials (COR-I [greenway2010], COR-II [apovian2013], COR-BMOD [wadden2011], COR-Diabetes [hollander2013]) totaling over 4,500 participants, plus a partial cardiovascular outcomes trial (LIGHT [nissen2016]) terminated early. Effect sizes for weight loss are consistent across trials (4, 5% placebo-adjusted at 56 weeks) and consistent with mechanism [saunders2016]. Independent network meta-analyses by Khera and colleagues (28 RCTs, 29,018 patients) [khera2016] and Singh and colleagues [singh2020] place naltrexone-bupropion mid-pack among approved obesity pharmacotherapies for absolute weight loss, behind liraglutide and phentermine-topiramate but ahead of orlistat and lorcaserin (since withdrawn) [caixas2014]. Onakpoya and colleagues' 2020 systematic review of unpublished clinical study reports reached similar effect-size conclusions and also documented adverse-event patterns consistent with the published trial reports [onakpoya2020] [yanovski2014; heymsfield2017].

Major society guidelines incorporate naltrexone-bupropion: the Endocrine Society's 2015 clinical practice guideline [apovian2015_guideline] and the AACE/ACE 2016 comprehensive clinical practice guidelines for medical care of patients with obesity [garvey2016_aace] both include the combination among recommended pharmacotherapy options for chronic weight management [caixas2014]. Broad reviews of the obesity-pharmacotherapy field place naltrexone-bupropion in context relative to the broader class.

Real-world evidence beyond the registration trials is limited but emerging: Ard and colleagues' 2024 telehealth-cohort analysis reported 12-month weight-loss outcomes for FDA-approved anti-obesity medications including naltrexone-bupropion under contemporary prescribing patterns [ard2024_realworld]. In-vivo functional MRI data from Wang and colleagues provide mechanistic confirmation in humans of altered reward-circuit connectivity on therapy [wang2018_fmri] [velazquez2018].

Evidence specifically supporting the compounded preparation is absent, there is no parallel efficacy program for compounded oral capsules. Compounded use is therefore an extrapolation from the manufactured-product evidence base, justified case by case by patient-specific clinical factors that the manufactured product cannot accommodate. The component drugs themselves have decades of safety data: bupropion since 1985 in MDD and 1997 for smoking cessation [hurt1997], with PK characterized in detail [hsyu1997] and a well-documented dose-related seizure-risk profile [davidson1989, pesola2002]; naltrexone since 1984 in opioid-use disorder and the early-1990s alcohol-use disorder approval [volpicelli1992], with PK characterized in the foundational Verebey work [verebey1976] [caixas2014].

Major Naltrexone-Bupropion Combination Clinical Studies

Study	Design	Participants	Duration	Finding
COR-I (Greenway 2010, Lancet)	Phase III, randomized, double-blind, placebo-controlled	1742	56 weeks	6.1% mean weight loss (high-dose combined therapy) vs 1.3% placebo; 48% vs 16% achieved ≥5% weight loss [greenway2010]
COR-II (Apovian 2013)	Phase III, randomized, double-blind, placebo-controlled	1496	56 weeks	6.4% mean weight loss vs 1.2% placebo; replicated COR-I efficacy [apovian2013]
COR-BMOD (Wadden 2011)	Phase III, randomized, double-blind, placebo-controlled with intensive behavioral modification arm	793	56 weeks	9.3% mean weight loss with combined therapy + BMOD vs 5.1% with placebo + BMOD [wadden2011]
COR-Diabetes (Hollander 2013)	Phase III, randomized, double-blind, placebo-controlled in adults with T2D	505	56 weeks	5.0% mean weight loss vs 1.8% placebo; HbA1c reduction 0.6% vs 0.1% [hollander2013]
LIGHT (Nissen 2016)	Cardiovascular outcomes RCT terminated early;	—	Interim follow-up	No statistically significant cardiovascular benefit established

Study	Design	Participants	Duration	Finding
	published interim analysis		(terminated early)	in interim data; trial did not exclude harm [nissen2016]
Anderson et al. (2002, Obesity Research)	Bupropion monotherapy, 48-week double-blind placebo-controlled trial in obese adults	327	48 weeks	Bupropion SR 300 mg/day produced 7.2% weight loss vs 5.0% placebo; 46% vs 30% achieved ≥5% weight loss, established the bupropion-monotherapy effect that motivated the combination [anderson2002]
Khera et al. (2016, JAMA)	Network meta-analysis of pharmacological treatments for obesity	28 RCTs, 29,018 patients	≥1 year	Naltrexone-bupropion produced ~5.0 kg placebo-adjusted weight loss; placed mid-pack among approved obesity pharmacotherapies (liraglutide and phentermine-topiramate produced larger effects) [khera2016]
Caixàs et al. (2014, Drug Des Devel Ther)	Comprehensive clinical review of all naltrexone SR/bupropion SR data through FDA approval	—	Pooled phase II, III data	Consistent 4, 5% placebo-adjusted weight reduction across the COR program; tolerability profile dominated by nausea (most concentrated in titration weeks) [caixas2014]
Volpicelli et al. (1992, Arch Gen Psychiatry)	Foundational RCT of naltrexone in alcohol use disorder	70	12 weeks	Naltrexone 50 mg/day reduced alcohol-relapse rate vs placebo, established naltrexone's clinical activity at the mu-opioid receptor and the dose precedent later carried into the combination [volpicelli1992]
Hurt et al. (1997, NEJM)	Pivotal RCT of sustained-release bupropion for smoking cessation	615	7 weeks treatment, 1 year follow-up	Bupropion SR 100, 300 mg/day produced dose-dependent quit-rate increases, established the bupropion SR formulation later combined with naltrexone [hurt1997]
Greenway et al. (2009, J Clin	Randomized, double-blind, placebo-controlled phase 2	419	24 weeks	Combined bupropion (400 mg/day) + naltrexone produced significantly greater weight loss

Study	Design	Participants	Duration	Finding
Endocrinol Metab), phase 2 RCT	comparing combined bupropion + naltrexone to each monotherapy and placebo			than either monotherapy or placebo, with the largest effect at the bupropion-400 + naltrexone-32 mg dose; supported dose selection for COR phase III [greenway2009_phase2]
Wang et al. (2018, Int J Obes), fMRI mechanism	Randomized double-blind placebo-controlled fMRI study of combined naltrexone + bupropion vs placebo	40	4 weeks	Combined therapy altered resting-state functional connectivity in hypothalamus and reward-circuit regions in directions consistent with reduced food-cue reactivity, in-vivo human confirmation of the rational-design hypothesis [wang2018_fmri]
Wang & Volkow et al. (2001, Lancet)	PET imaging of striatal dopamine D2-receptor availability in adults with severe obesity vs lean controls	20	Cross-sectional	Striatal D2-receptor availability inversely correlated with BMI in severely obese adults, established the dopamine reward-circuit deficit that informed the rationale for catecholamine-modulating obesity pharmacotherapy [wang2001]
Singh et al. (2020, Expert Rev Clin Pharmacol)	Systematic review and meta-analysis of RCTs of pharmacotherapy in obesity	Multiple RCTs across all approved AOMs	≥12 months follow-up	Confirmed naltrexone-bupropion produces 4, 5% placebo-adjusted weight loss; GLP-1 receptor agonists and phentermine-topiramate produced larger absolute effects [singh2020]
Onakpoya et al. (2020, Br J Clin Pharmacol)	Systematic review and meta-analysis using unpublished clinical study reports	Four phase III RCTs (COR program)	Up to 56 weeks	Confirmed published weight-loss effect sizes from clinical study reports; also documented adverse-event rates and discontinuation patterns consistent with published trial reports [onakpoya2020]
Hsyu et al. (1997, J Clin Pharmacol), bupropion PK	Single- and multiple-dose pharmacokinetic study of bupropion and its metabolites in smokers and nonsmokers	24	Single-dose and 14-day multiple-dose phases	Characterized bupropion's primary metabolic disposition via CYP2B6 to hydroxybupropion (longer half-life than parent), threohydrobupropion, and erythrohydrobupropion, informed

Study	Design	Participants	Duration	Finding
				the combination's drug-interaction labeling [hsyu1997]
Verebey et al. (1976, Clin Pharmacol Ther), naltrexone PK	Pharmacokinetic and pharmacodynamic study of naltrexone after acute and chronic oral dosing	Healthy and former opioid-dependent volunteers	Acute single-dose and chronic dosing	Characterized naltrexone disposition: oral bioavailability with extensive first-pass conversion to 6β-naltrexol; parent half-life ~4 h and 6β-naltrexol half-life ~13 h sustains receptor occupancy across the dosing interval [verebey1976]
Pesola & Avasarala (2002, J Emerg Med), bupropion seizure risk	Emergency department case series and review of new-onset and drug-related generalized seizures	—	ED case series review	Bupropion was a disproportionately represented drug-related cause of new-onset generalized seizures presenting to the ED, supports the seizure-risk dose ceiling carried into the naltrexone-bupropion combination [pesola2002]
Apovian et al. (2015, J Clin Endocrinol Metab), Endocrine Society guideline	Clinical practice guideline using GRADE methodology	—	N/A	Endocrine Society recommends pharmacotherapy (including naltrexone-bupropion) as adjunct to lifestyle modification in adults with BMI ≥30 or ≥27 with weight-related comorbidity; outlines selection considerations across approved agents [apovian2015_guideline]
Garvey et al. (2016, Endocr Pract), AACE/ACE guidelines	Comprehensive clinical practice guideline (AACE/ACE)	—	N/A	AACE/ACE comprehensive obesity-management guidelines include naltrexone-bupropion as one of the recommended chronic weight-management pharmacotherapies, with selection guided by comorbidity profile and tolerability [garvey2016_aace]
Yanovski & Yanovski (2014, JAMA)	Systematic and clinical review of long-term obesity pharmacotherapy	—	Reviewed long-term RCT evidence	Reviewed efficacy and safety of long-term obesity drug treatment including naltrexone-bupropion and contextualized effect sizes against orlistat, phentermine-

Study	Design	Participants	Duration	Finding
				topiramate, and lorcaserin [yanovski2014]
Heymsfield & Wadden (2017, NEJM)	Narrative review of mechanisms, pathophysiology, and management of obesity	—	N/A	Placed naltrexone-bupropion within the broader pharmacotherapy landscape and detailed the POMC-arcuate mechanism that underpins the combination [heymsfield2017]
Ard et al. (2024, Obesity), real-world telehealth cohort	Retrospective real-world analysis of a telehealth obesity-treatment provider using FDA-approved AOMs	—	12 months	Documented 12-month weight-loss outcomes across FDA-approved anti-obesity medications including naltrexone-bupropion in contemporary telehealth prescribing, first large real-world AOM cohort to include the combination [ard2024_realworld]
Tek (2016, Patient Prefer Adherence)	Clinical review of naltrexone-bupropion focused on patient selection and persistence	—	N/A	Reviewed the COR-program persistence and tolerability data; emphasized titration pacing as the primary lever for first-month tolerability and adherence [tek2016]

Naltrexone-Bupropion Combination Pharmacokinetics & Pharmacodynamics

Pharmacokinetics

Manufactured Contrave is formulated as sustained-release tablets [fda_label_contrave]. Bupropion Tmax approximately 3 hours; naltrexone Tmax approximately 2 hours. Bupropion half-life approximately 21 hours (with active metabolites contributing) [hsyu1997]; naltrexone half-life approximately 4, 5 hours for the parent and ~13 hours for the active metabolite 6β-naltrexol [verebey1976].

Both components are extensively metabolized: bupropion primarily by CYP2B6 to the active metabolite hydroxybupropion (longer half-life than parent) and to threohydrobupropion and erythrohydrobupropion as characterized by Hsyu and colleagues [hsyu1997]; naltrexone primarily by dihydrodiol dehydrogenase to 6β-naltrexol as characterized by Verebey and colleagues [verebey1976]. Renal excretion of metabolites

predominates for both. Steady-state is reached after approximately 7 days at maintenance dosing [fda_label_contrave].

Compounded immediate-release oral capsules will not replicate the sustained-release PK of the manufactured tablet. Cmax with compounded capsules is expected to be higher and Tmax shorter; this affects both efficacy timing and tolerability profile and should inform titration decisions.

Pharmacodynamics

Pharmacodynamic effects are dominated by sustained suppression of appetite signaling and reduction in food craving, particularly for highly palatable foods. Behavioral measures from COR-BMOD subset analyses showed reductions in self-reported food craving and binge-eating tendencies that paralleled weight loss in the combined-therapy arm [wadden2011].

Cardiovascular pharmacodynamics include modest sustained increases in heart rate (approximately 1 bpm) and blood pressure (approximately 1 mmHg systolic) in pooled COR data, attributed to the bupropion component's noradrenergic activity [fda_label_contrave]. These effects warrant baseline and on-therapy blood-pressure monitoring.

↓↑ Comparing Naltrexone-Bupropion Combination Formulations

The manufactured Contrave tablet is a sustained-release matrix engineered to deliver naltrexone and bupropion in a controlled-release profile that supports twice-daily dosing at steady state [fda_label_contrave]. This formulation has been the subject of all phase III efficacy and safety data.

Compounded immediate-release oral capsules differ pharmacokinetically. They produce higher peak concentrations and shorter dosing intervals are needed to maintain steady-state. Patients switched from manufactured to compounded preparations (or vice versa) should be re-evaluated for dose titration and tolerability; equivalence cannot be assumed.

RonanRx-compounded preparations are dispensed only when the manufactured product is not appropriate for the identified patient. The pharmacist review documents the patient-specific clinical reason and the resulting formulation difference is noted on dispensing.

🌡 Naltrexone-Bupropion Combination Storage and Handling

Compounded oral capsules are stored at controlled room temperature (USP definition: 20, 25°C, with allowed excursions 15, 30°C) in tightly closed light-resistant containers. Beyond-use date is established per USP <795> for non-sterile compounding, typically up to 180 days for solid oral formulations from non-sterile components, subject to formulation-specific stability data [usp_795].

Manufactured Contrave is similarly stored at 20, 25°C with excursions permitted to 15, 30°C. Both bupropion and naltrexone are stable as their HCl salts at room temperature; no refrigeration is required for compounded oral capsules [fda_label_contrave].

Naltrexone-Bupropion Combination Compounding & Operations

503A compounding

Compounded naltrexone-bupropion is prepared under 503A on patient-specific prescriptions in state-licensed compounding pharmacies. RonanRx prepares non-sterile oral capsules per USP General Chapter <795>, the official compendial standard for non-sterile pharmaceutical compounding, with documented active ingredient sourcing (USP/NF grade where available), gravimetric verification, and finished-product quality checks per the pharmacy's quality-management system [fda503a; usp_795].

Beyond-use dating, ingredient identity verification, and stability assessment follow USP <795> requirements. Each compounded batch is documented per state board of pharmacy retention rules with full traceability from API lot through dispensing.

Pharmacist review

Each prescription for compounded naltrexone-bupropion undergoes pharmacist review prior to dispensing. The review confirms: a documented patient-specific clinical reason that the manufactured Contrave is not appropriate (excipient sensitivity, dose individualization, supply gap, or other documented factor); absence of contraindications (seizure disorder, eating disorder, chronic opioid use, uncontrolled hypertension, pregnancy); and the prescribed regimen aligns with FDA-label dose ceilings.

RonanRx does not fill prescriptions that read as routine substitution of compounded for manufactured product without documented clinical rationale, consistent with FDA guidance on compounded copies of commercially available drugs [fda_essentially_a_copy].

Quality and traceability

Active pharmaceutical ingredients are sourced from FDA-registered facilities with documented certificates of analysis. Each batch is recorded with lot numbers traceable to API source, compounding date, beyond-use date, and dispensing pharmacist of record. Finished product lot records are retained per state board of pharmacy retention requirements.

Cold chain

Compounded oral capsules of naltrexone-bupropion are not cold-chain products. They are stable at controlled room temperature and shipped in standard pharmacy-grade packaging. Patients should store at room temperature in tightly closed containers away from heat and humidity, consistent with the manufactured Contrave label.

Frequently Asked Questions About Naltrexone-Bupropion Combination

Is compounded naltrexone-bupropion the same as Contrave?

No. Contrave is the FDA-approved manufactured product (naltrexone 8 mg / bupropion 90 mg sustained-release tablet) [fda_label_contrave]. Compounded preparations are pharmacy-prepared on a patient-specific prescription and are not bioequivalent to Contrave. Compounded drugs are not FDA-approved [fda503a].

When is a compounded version appropriate?

Per FDA guidance, a compounded version of an FDA-approved drug is generally restricted unless the prescriber documents a patient-specific clinical need that the manufactured product cannot meet, for example, excipient sensitivity, dose individualization outside the manufactured strength, or a documented manufactured-product supply gap [fda_essentially_a_copy].

How well does naltrexone-bupropion work for weight loss?

In the manufactured-product COR phase III program, mean placebo-adjusted weight loss was 4, 5% at 56 weeks [greenway2010; apovian2013; wadden2011]. Approximately 48% of completers in the combined-therapy arm of COR-I achieved ≥5% body-weight loss vs 16% on placebo. Effect sizes are similar across the four trials and consistent across populations including type 2 diabetes [hollander2013].

What are the most common side effects?

Nausea, constipation, headache, vomiting, dizziness, and insomnia, mostly mild to moderate and concentrated in the first 4, 8 weeks of titration. Approximately 24, 28% of patients in the COR program discontinued for adverse events vs 12, 14% on placebo [greenway2010; apovian2013].

Who should not take naltrexone-bupropion?

Contraindicated in seizure disorder, current or past bulimia or anorexia, chronic opioid use, abrupt discontinuation of alcohol or sedatives, uncontrolled hypertension, MAO-inhibitor use within 14 days, pregnancy, and known allergy to either component. Patients requiring acute opioid analgesia (e.g., postoperative) should not be on therapy [fda_label_contrave].

Does RonanRx sell compounded naltrexone-bupropion directly to patients?

No. Compounded naltrexone-bupropion requires a patient-specific prescription written by a licensed doctor for an identified patient with a documented clinical reason that the manufactured Contrave is not appropriate, plus pharmacist review before dispensing [fda_essentially_a_copy]. RonanRx is not a direct-to-consumer storefront [fda503a].

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How to Access Naltrexone-Bupropion Combination

Compounded Naltrexone-Bupropion Combination is dispensed under 503A on a patient-specific prescription. Depending on your role, the next step looks different.

FOR PRESCRIBING CLINICIANS

Offer this medication

A pharmacist will follow up within two business days. We'll cover state availability, supported formulations, and what integration looks like for your clinic.

ronanrx.com/request-partnership-call

PATIENT WITH A DOCTOR

Receive your prescription

If your doctor has prescribed Naltrexone-Bupropion Combination, sign up so we can prepare and ship your medication. The signup wizard collects intake and connects you to the prescribing workflow.

ronanrx.com/patients

PATIENT WITHOUT A DOCTOR

Find a partner clinic

RonanRx prescribes through partner clinics — we don't initiate prescriptions on this site. Read how the referral process works and how to find a partner clinic in your state.

ronanrx.com/find-clinic

Other compounds RonanRx makes

This monograph is one of many in the RonanRx formulary. Every compound below is prepared under 503A on a patient-specific prescription. Browse the full catalog at ronanrx.com/medications and ronanrx.com/peptides, or scan the codes at right for each index.

Medications

Peptides

MEDICATIONS (40)

Alpha-Lipoic Acid (ALA) — Antioxidant & mitochondrial
Coenzyme Q10 (CoQ10) — Antioxidant & mitochondrial
Glutathione — Antioxidant & mitochondrial
NAD+ / NMN — Antioxidant & mitochondrial
Compounded Topical Anesthetics (BLT, LET) — Dermatology
Topical Minoxidil — Dermatology
Topical Tretinoin — Dermatology
Compounded Magnesium — Energy & nutritional
Cyanocobalamin — Energy & nutritional
High-Dose Vitamin D — Energy & nutritional
Hydroxocobalamin — Energy & nutritional
Iron (Compounded) — Energy & nutritional
L-Carnitine — Energy & nutritional
Methylcobalamin (B12) — Energy & nutritional
Methylfolate — Energy & nutritional
Anastrozole — Hormone optimization
Clomiphene & Enclomiphene — Hormone optimization
DHEA — Hormone optimization
Estradiol — Hormone optimization
Estriol — Hormone optimization
Human Chorionic Gonadotropin (HCG) — Hormone optimization
Pregnenolone — Hormone optimization
Progesterone — Hormone optimization
Testosterone — Hormone optimization
Compounded Metformin — Metabolic & weight
Compounded Semaglutide — Metabolic & weight
Compounded Tirzepatide — Metabolic & weight
Lipotropic Injection (MIC, MICC) — Metabolic & weight
Low-Dose Naltrexone (LDN) — Metabolic & weight
Naltrexone-Bupropion Combination — Metabolic & weight
Topiramate — Metabolic & weight
Bremelanotide / PT-141 — Sexual health
Compounded Sildenafil — Sexual health
Compounded Tadalafil — Sexual health
Trimix Injection — Sexual health
Compounded Gabapentin — Sleep & recovery
Compounded Melatonin — Sleep & recovery
Compounded T3 (Liothyronine) — Thyroid
Compounded T3/T4 Combinations — Thyroid
Compounded T4 (Levothyroxine) — Thyroid

PEPTIDES (21)

Sermorelin — Available now

Tesamorelin — Available now

AOD-9604 — Growth-hormone axis (under FDA review)

CJC-1295 — Growth-hormone axis (under FDA review)

GHRP-2 / GHRP-6 — Growth-hormone axis (under FDA review)

Hexarelin — Growth-hormone axis (under FDA review)

Ipamorelin — Growth-hormone axis (under FDA review)

MK-677 / Ibutamoren — Growth-hormone axis (under FDA review)

5-Amino 1MQ — Metabolic & longevity (under FDA review)

Epitalon / Epithalon — Metabolic & longevity (under FDA review)

MOTS-C — Metabolic & longevity (under FDA review)

Thymosin Alpha-1 / Thymalin — Metabolic & longevity (under FDA review)

DSIP, Delta Sleep-Inducing Peptide — Neuro & cognitive (under FDA review)

Selank — Neuro & cognitive (under FDA review)

Semax — Neuro & cognitive (under FDA review)

Vasoactive Intestinal Peptide (VIP) — Neuro & cognitive (under FDA review)

BPC-157 — Tissue repair (under FDA review)

KPV — Tissue repair (under FDA review)

LL-37 — Tissue repair (under FDA review)

Pentadeca Arginate (PDA) — Tissue repair (under FDA review)

TB-500 / Thymosin Beta-4 — Tissue repair (under FDA review)