Calocurb® CLINICAL

CLINICAL APPLICATIONS

- Reduces Appetite and Food Cravings
- Supports Long-Term Weight Management
- Stimulates Natural GLP-1, CCK and PYY Release
- Complements Lifestyle and Pharmaceutical Weight Loss Strategies
- Enhances Adherence to Intermittent Fasting and Time-Restricted Eating



PRACTITIONER-EXCLUSIVE

Calocurb® CLINICAL is a practitioner-exclusive supplement that supports appetite control by working with the body's natural hormonal signals. It features Amarasate®, a clinically studied extract of New Zealand bitter hops, delivered in a delayed-release capsule designed to reach the small intestine where it activates bitter taste receptors. This triggers the release of key satiety hormones including GLP-1, CCK and PYY, which work together to significantly reduce hunger, cravings, and caloric intake. Fast-acting and plant-based, Calocurb® CLINICAL offers a targeted, science-driven approach to supporting healthy weight management.

OVERVIEW

Successful weight management is now a global health concern as more than 43% of adults are categorized as overweight or obese.¹ Long term weight management requires lifestyle modification but often includes higher-force interventions such as pharmaceutical or surgical care. Pharmaceutical interventions are usually designed to reduce food intake by manipulating appetite; however, these interventions have long-term feasibility or safety concerns.²-³ Naturally derived compounds, with favorable safety profiles and the ability to powerfully suppress appetite and cravings, represent an appealing option for ongoing weight management.

Appetite regulation is orchestrated by a complex network of physical and chemical signals, with enteroendocrine hormones serving as some of the most powerful drivers of hunger and satiety. Under normal physiology, orexigenic hormones such as ghrelin rise during fasting and between meals, while anorexigenic hormones including GLP-1,

CCK and PYY are released after eating. Specialized enteroendocrine cells in the gastrointestinal tract release these hormones in a dose- and time-dependent manner in response to nutrient intake.⁴

Bitter plant compounds have long been recognized for their role in modulating appetite. Historically, certain cultures intentionally consumed bitter plants to help manage hunger during extended travel or periods of limited food availability. These compounds stimulate bitter (TAS2R) receptors located throughout the gastrointestinal tract, triggering an enhanced anorexigenic hormone response (GLP-1, CCK and PYY). Activation of these receptors by non-toxic bitter plant extracts can support optimal appetite regulation, providing a natural, targeted strategy for modern weight management.

BACKGROUND

In 2010, the New Zealand government funded a large grant to investigate the appetite suppressive effects of bitter plant compounds as a potential treatment option for weight management. After investigating over 1,000 different plant compounds in vitro, the researchers concluded that a native New Zealand hops extract produced the strongest TAS2R stimulation and consequential enhanced release of anorexigenic (GLP-1, CCK and PYY) hormonal response, indicating the strongest appetite suppressant effect. The researchers named the extract Amarasate®, derived from Latin, meaning "bitter satiation."

In 2019, the first clinical study on Amarasate® was conducted in a randomized, double-blind trial investigating its appetite suppressive effects during a 24-hour,

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water-only fast. Participants given Amarasate® or placebo at hours 16 and 20 were evaluated for hunger and satiety with a standard visual analog scale (VAS) every 30 minutes after capsule administration. Amarasate® participants reported an 80% reduction in hunger elevation scores compared to the placebo group.8 In a comparable water-fast study conducted in women, Amarasate® supplementation led to a 100% suppression of hunger elevation and a 120% reduction in food cravings relative to placebo.9

A more expansive study of adult men sought to correlate the subjective reduction in hunger from the first study with anorexigenic biomarkers, specifically GLP-1, CCK and PYY. The study also sought to investigate which was more efficacious, intragastric or intraduodenal delivery of Amarasate[®]. In the randomized, double-blind study, the subjects were given either placebo, intraduodenal Amarasate[®] (delayed-release capsule), or intragastric Amarasate[®] (immediate-release capsule) one hour before an *ad libitum* meal and subsequent snack. Both Amarasate[®] delivery methods had significant elevations in GLP-1,

CCK and PYY; however, the intragastric capsule also had significantly more adverse events than the intraduodenal capsule likely due to the high amount of TAS2R bitter receptors in the stomach. Intraduodenal delivery of Amarasate® resulted in 600% elevation from baseline of GLP-1 and CCK, and 50% elevation of PYY.¹⁰

CLINICAL CONSIDERATIONS

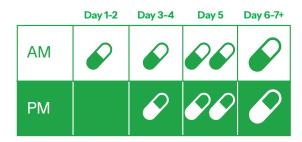
Amarasate® is a potent and effective appetite modulator, offering a targeted approach to supporting satiety and caloric control. It can be used independently or integrated into a comprehensive strategy for weight loss or maintenance. Calocurb® CLINICAL may be co-administered with weight-loss medications to help manage breakthrough hunger or used during medication tapering to support appetite control. Alternatively, Calocurb® CLINICAL can also be used as needed to support adherence to time-restricted eating or to help manage appetite and craving increases that may occur premenstrually.

Directions for Use

CLINICAL STARTER PACK

Contains: 10 x 125 mg capsules and 50 x 250 mg capsules

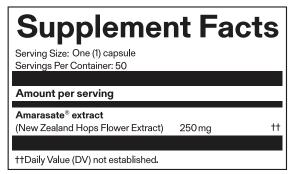
Patients should begin Calocurb® CLINICAL using the Starter Pack. This pack onboards the body to the increased activation of natural satiety hormones.



- Day 1-2: Take one 125 mg capsule one hour before a meal.
- **Day 3-4:** Take one 125 mg capsule, twice daily, one hour before a meal.
- **Day 5:** Take two 125 mg capsules, twice daily, one hour before a meal.
- **Day 6-7+:** Take one 250 mg capsule, twice daily, one hour before a meal.

Always take on an empty stomach with a minimum of 8 ounces of water.

Supplement Facts Serving Size: One (1) capsule Servings Per Container: 10 Amount per serving Amarasate® extract (New Zealand Hops Flower Extract) 125 mg ### ##Daily Value (DV) not established.



Other Ingredients: Canola oil (non GMO and Glyphosate free), Rosemary leaf extract, Vegetarian Capsule (Hypromellose)

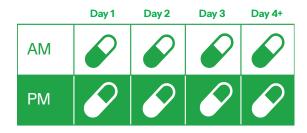
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Directions for Use

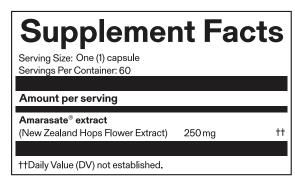
CLINICAL MAINTENANCE PACK

Contains: 60 x 250 mg capsules

Patients should continue on a dose of Calocurb® CLINICAL 250 mg twice daily, using the Maintenance Pack.



Take one 250 mg capsule, twice daily, one hour before a meal. Always take on an empty stomach with a minimum of 8 ounces of water.



Other Ingredients: Canola oil (non GMO and Glyphosate free), Rosemary leaf extract, Vegetarian Capsule (Hypromellose)

DOES NOT CONTAIN

Sugar, starch, yeast, wheat, gluten, soy, milk, eggs, shellfish, fish, peanuts, tree nuts. No artificial colors, flavors or preservatives.

CAUTIONS

This product is not intended for pregnant or nursing women or for persons under 18. Consult your healthcare professional prior to use if you have or suspect a medical condition or are taking prescription drugs. Discontinue use and seek advice of a doctor if any adverse reactions occur.

References

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- 3. Christofferson BØ, Sanchez-Delgado G, John LM, Ryan DH, Raun K, Ravussin E. Beyond appetite regulation: Targeting energy expenditure, fat oxidation, and lean mass preservation for sustainable weight loss. Obesity (Silver Spring) 2022;30(4):841-857.
- 4. Holliday A, Horner K, Johnson KO, Dagbasi A, Crabtree DR. Appetite-related Gut Hormone Responses to Feeding Across the Life Course. J Endocr Soc 2025;9(2):bvae223.
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- 6. Nissim I, Dagan-Wiener A, Niv MY. The taste of toxicity: A quantitative analysis of bitter and toxic molecules. IUBMB Life 2017;69(12):938-946.
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- $\textbf{8.} \ \text{Walker E, Lo K, Tham S, et al. New Zealand bitter hops extract reduces hunger during a 24 h water only fast. \\ \textit{Nutrients} 2019;11(11):2754.$
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