



Weight to Go: Naltrexone/bupropion for weight loss

CLINICAL QUESTION

Is naltrexone/bupropion (Contrave[®]) effective for weight loss?

BOTTOM LINE

Over 28-56 weeks, at best, ~50% of patients taking naltrexone/bupropion achieved a >5% loss in body weight, compared to ~20% in control. Naltrexone/bupropion adverse events (examples nausea, constipation) lead to withdrawal in 23% of patients versus 12% on placebo.

EVIDENCE

- Focused on systematic reviews with meta-analysis of randomized, placebo-controlled trials (RCTs). Results statistically significant unless noted.
- Systematic review, 4 RCTs, 3955 patients who received at least one dose, baseline weight 100kg.¹ Both arms included lifestyle changes (e.g., 500kcal/day deficit, increase activity). Naltrexone-bupropion (titrated to 16/180mg BID) versus placebo. At 56 weeks:
 - Participants with ≥5% weight loss: Naltrexone/bupropion 53% versus placebo 21%, number needed to treat (NNT)=4.
 - ≥10% weight loss: Naltrexone/bupropion 29% versus placebo 9%, NNT=5.
 - Mean weight loss (2 RCTs reporting): ~ 6 kg versus ~1 kg control.
 - Withdrawals due to adverse effects: 25% versus 13% placebo, number needed to harm (NNH)=8.
 - Other systematic reviews found similar.²⁻⁴

- Systematic review, same 4 RCTs as above except included lower dosage arm (8/180mg BID) and used all randomized participants, 4536 patients.⁵
 - Outcomes at 28-56 weeks:
 - ≥5% weight loss: Naltrexone/bupropion 38% versus placebo 17%, NNT=5.
 - ≥10% weight loss: Naltrexone/bupropion 22% versus placebo 8%, NNT=8.
 - Mean weight loss: ~4.5kg versus 2kg (placebo).
 - Withdrawals due to adverse events: 23% versus 12% (placebo), NNH=10.
 - Most common adverse events include nausea (31% versus 7% placebo) and constipation (18% versus 7% placebo).
- Limitations: All RCTs were industry funded, high dropout rates (~45%), inconsistent magnitude of effects across RCTs but all showed benefit.

CONTEXT

- Trial looking at cardiovascular safety stopped early due to data breach, however, systematic review of 5 RCTs found no association with cardiovascular events.⁶⁻⁷
- Weight regain after stopping medication unknown.
- Cost (1 month)⁸: ~\$350 (generally not covered). Off-label prescribing of individual components at lower doses ~\$80.⁹
- Other medications for weight loss include (with mean weight loss in RCTs): Orlistat (~2.6kg)¹ or GLP-1 agonists such as semaglutide (~10-15kg)¹⁰ or liraglutide (~5kg)¹¹. Baseline weight in studies ~101-106kg.

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AUTHORS

Betsy Thomas, BSc Pharm,
Adrienne J Lindblad, BSP ACPR
 PharmD, **Thao Luu**, BSc Pharm
 PharmD candidate, **Allison
 Paige**, MD CCFP

*Authors do not have any conflicts
 of interest to declare.*

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