# Q/ Is immediate-release topiramate an effective treatment for adult obesity?

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## EVIDENCE-BASED ANSWER

A/ **Yes.** Topiramate (at daily doses of 64-400 mg) produces an average 5.34 kg of additional weight loss compared with placebo (95% confidence interval [CI], -6.12 to -4.56) in overweight to obese adults for periods of 16 to 60 weeks (strength of recommendation [SOR]: **A**, meta-analyses of randomized controlled trials [RCTs]).

Topiramate increases the chances of losing 5% or more of baseline body weight (BBW) with a number needed to treat (NNT) of 3 (95% CI, 2-3) and 10% or more of BBW with an NNT of 4 (95% CI, 3-4). However, approximately 17% of patients discontinue the drug because of adverse effects, including paresthesia, hypoesthesia, taste perversion, and psychomotor impairment (SOR: **A**, meta-analyses of RCTs).

## Evidence summary

A meta-analysis of 10 well-done RCTs with a total of 3320 patients found that topiramate produced more weight loss than placebo.[1] Studies included men and women ages 18 to 75 years, with a body mass index (BMI) of 27 to 50. Several studies included patients with hypertension, dyslipidemia, and diabetes mellitus; one study included patients with binge eating disorder. Investigators recruited subjects from sites in Europe, North America, Australia, and South Africa. The studies lasted 16 to 60 weeks and used variable doses of topiramate (64-400 mg daily). Most incorporated a structured lifestyle intervention program for both the treatment and control groups.

Patients taking topiramate lost 5.34 kg (95% CI, -6.12 to -4.56) more than subjects taking placebo. All studies showed significantly greater weight loss in the topiramate groups, regardless of dose and duration, although there was some heterogeneity among the results. The NNTs to achieve weight loss of 5% or more of BBW and 10% or more of BBW were 3 (95% CI, 2-3) and 4 (95% CI, 3-4), respectively.

### No major adverse events, but some unpleasant effects

A safety analysis on 6620 subjects found no major adverse events.[1] Subjects in the topiramate group were more likely to withdraw because of adverse effects (odds ratio=1.97; 95% CI, 1.64-2.29; number needed to harm=14; 95% CI, 11-18). The most common adverse effects were paresthesia, hypoesthesia, taste perversion, and psychomotor impairment, and these effects were most likely to lead to discontinuation at daily doses >96 mg.

### Two formulas are effective in patients with diabetes

Investigators stopped 6 studies early because the sponsor wanted to pursue development of a controlled-release formulation of topiramate. The meta-analysis includes a single study of controlled-release topiramate, 175 mg daily in patients with diabetes, that showed equivalent efficacy and similar tolerability to immediate-release topiramate.[2]

Three other RCTs included in the meta-analysis specifically examined obese pa-

tients with type 2 diabetes, a population deemed more resistant to typical weight loss regimens, treated with immediate-release topiramate in dosages of 96 mg and 192 mg daily.[3-5] These patients also experienced greater weight loss than patients taking placebo, comparable to what was seen in the overall meta-analysis.

### FDA approval and cost of therapy

Topiramate monotherapy isn't approved by the US Food and Drug Administration (FDA) for obesity treatment. In 2012, the FDA approved phentermine/topiramate extended-release (Qsymia) for long-term treatment of obesity; the monthly cost for a maintenance dose of 7.5 mg/46 mg daily is approximately $185.[6] Topiramate immediate-release tablets cost approximately $25 per month for twice daily doses of 50 to 100 mg.[7]

## Recommendations

The US Preventive Services Task Force recommends screening all adults for obesity by measuring BMI and referring patients with a BMI ≥30 for high-intensity, comprehensive behavioral interventions. It makes no recommendation for pharmacologic management.[8]

The Institute for Clinical Systems Improvement concludes that pharmacotherapy should be used only as part of a comprehensive obesity treatment plan. Pharmacotherapy should be considered if obese patients are unable to lose 1 pound per week with diet, physical activity, and behavior modification.[9] JFP


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