ACP Issues Guidance on Medications for Obesity, Overweight

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The management of obesity and overweight presents a persistent clinical challenge, with lifestyle interventions often yielding modest and unsustained weight reduction. Clinicians frequently encounter questions regarding the appropriate use of pharmacologic agents to support weight management. The American College of Physicians (ACP) has now issued guidance on medications for obesity and overweight, providing a framework for their application in adult patients.

KEY TAKEAWAYS

- The Pivot: The ACP guidance provides a structured approach to pharmacotherapy for obesity and overweight, emphasizing specific patient populations and treatment durations.
- The Data: The guidance highlights that pharmacologic interventions can achieve an average weight reduction of 5% to 10% of baseline body weight.
- The Action: Clinicians should consider pharmacotherapy for adults with obesity (BMI e30 kg/m2) or overweight (BMI e27 kg/m2) with weight-related complications, in conjunction with lifestyle modifications.

Obesity and overweight are chronic conditions associated with numerous comorbidities, including type 2 diabetes, cardiovascular disease, and certain cancers. Lifestyle interventions, comprising dietary changes, increased physical activity, and behavioral therapy, are foundational to weight management. However, these interventions frequently result in limited long-term weight loss, prompting the consideration of pharmacologic adjuncts. The ACP guidance addresses the role of prescription therapies in adults with obesity or overweight and weight-related complications.

The global prevalence of obesity has steadily increased over the past several decades, posing a significant public health challenge. In the United States, more than two-thirds of adults are either overweight or obese, contributing to a substantial burden of chronic disease and healthcare expenditures. Effective management strategies are crucial to mitigate these health risks. While lifestyle modifications are the cornerstone of treatment, their efficacy in achieving and sustaining significant weight loss often proves challenging for many individuals due to complex biological, environmental, and behavioral factors that influence body weight regulation.

ACP Guidance on Pharmacologic Treatment

The ACP guidance recommends that clinicians offer pharmacologic treatment to adults with obesity (body mass index (BMI) e30 kg/m2) or overweight (BMI e27 kg/m2) who have weight-related complications, after lifestyle interventions have been implemented and found insufficient. The guidance emphasizes that these medications should be used as an adjunct to, not a replacement for, lifestyle modifications. The primary goal of pharmacotherapy is to achieve clinically

meaningful weight loss, defined as a reduction of at least 5% of baseline body weight, which has been associated with improvements in metabolic parameters and reduction in comorbidity risk.

The development of the ACP guidance involved a systematic review of existing evidence on the efficacy and safety of anti-obesity medications. The review focused on randomized controlled trials and observational studies involving adult populations. The panel considered various outcomes, including percentage of weight loss, improvements in weight-related comorbidities (e.g., glycemic control, blood pressure, lipid profiles), and the incidence of adverse events. The evidence synthesis informed the strength of recommendations and the quality of evidence ratings, ensuring a rigorous, evidence-based approach to clinical practice recommendations.

The guidance reviews several anti-obesity medicines, noting that most agents approved for long-term use demonstrate an average weight reduction of 5% to 10% of baseline body weight over 12 to 18 months. Specific agents discussed include glucagon-like peptide-1 (GLP-1) receptor agonists, such as liraglutide and semaglutide, which have shown efficacy in weight reduction and improvements in glycemic control. These agents primarily act by mimicking endogenous incretin hormones, enhancing glucose-dependent insulin secretion, slowing gastric emptying, and promoting satiety. Other agents, such as phentermine-topiramate extended-release and naltrexone-bupropion extended-release, are also considered. Phentermine-topiramate combines a sympathomimetic amine anorectic with an anticonvulsant, while naltrexone-bupropion combines an opioid antagonist with an antidepressant, both acting on central pathways to reduce appetite and cravings. The guidance stresses the importance of shared decision-making, discussing the potential benefits, risks, and side effects of each medication with patients.

A key aspect of the ACP guidance is the recommendation for discontinuation of pharmacotherapy if a patient does not achieve at least a 5% weight loss after 12 weeks of treatment at the maximum tolerated dose. This pragmatic approach aims to avoid prolonged exposure to medications that are not providing sufficient clinical benefit, thereby minimizing potential side effects and healthcare costs. The guidance also highlights the need for ongoing monitoring of patients receiving anti-obesity medicines for efficacy, tolerability, and adverse events. Long-term use of these medications is often necessary to maintain weight loss, as discontinuation can lead to weight regain.

The ACP guidance does not recommend specific medications over others but rather provides a framework for their appropriate use based on patient characteristics, comorbidities, and individual response. It underscores that the choice of medication should be individualized, considering factors such as patient preferences, contraindications, and potential drug interactions. For instance, patients with a history of cardiovascular disease may benefit from agents with demonstrated cardiovascular safety profiles. The guidance also acknowledges that bariatric surgery remains an option for patients with severe obesity (BMI ≥40 kg/m2) or BMI ≥35 kg/m2 with significant comorbidities, particularly when pharmacologic and lifestyle interventions have been unsuccessful. The guidance's limitations include its focus primarily on currently approved medications, potentially not encompassing future therapeutic advancements, and the inherent variability in patient response to pharmacotherapy, which necessitates careful clinical judgment beyond general recommendations.

Delve deeper into the complex endocrine and metabolic aspects of conditions discussed, including obesity, with the comprehensive Oxford Handbook of Endocrinology and Diabetes.

CLINICAL IMPLICATIONS

The ACP's guidance on pharmacologic treatment for obesity and overweight provides a necessary, if somewhat conservative, framework for clinicians. The emphasis on a 5% weight loss threshold for continuing therapy after 12 weeks is a practical measure. It should encourage prescribers to evaluate efficacy early and discontinue ineffective treatments, rather than prolonging exposure to agents that may carry side effects without delivering clinical benefit. This approach may help mitigate the financial burden on patients and healthcare systems, particularly given the high cost of newer GLP-1 receptor agonists.

For patients, this guidance reinforces that anti-obesity medicines are not standalone solutions but adjuncts to lifestyle changes. The expectation of a 5% to 10% weight reduction, while clinically meaningful, should be communicated clearly to manage patient expectations. The long-term nature of obesity management, often requiring continuous pharmacotherapy to prevent weight regain, also needs careful discussion. Patients should understand that these treatments are not a temporary fix but a sustained commitment, similar to managing hypertension or type 2 diabetes.

From an industry perspective, the ACP's measured stance, which does not explicitly endorse one drug class over another, suggests that the market for anti-obesity medicines will continue to be driven by efficacy, safety, and cost-effectiveness data. Companies developing or marketing GLP-1 receptor agonists, such as Novo Nordisk with semaglutide (Wegovy) and Eli Lilly with tirzepatide (Zepbound), will need to continue demonstrating robust outcomes beyond weight loss, particularly regarding cardiovascular benefits, to solidify their market position and justify premium pricing. The guidance implicitly encourages a competitive environment where evidence-based differentiation will be key.

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