Obesity Pharmacotherapy Beyond Weight Loss: Incretin-Based Therapies, Maintenance, and the Role of Family Physicians

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Abstract

According to the American Association of Clinical Endocrinology, obesity is a chronic disease driven by complex genetic, environmental, metabolic, and neuroregulatory factors that disrupt energy homeostasis and promote excess adiposity (1). This framing has shifted obesity treatment from short-term weight reduction toward long-term chronic disease management. Incretin-based therapies, including glucagon-like peptide-1 receptor agonists and dual glucose-dependent insulinotropic polypeptide/glucagon-like peptide-1 receptor agonists, have transformed medical obesity treatment, with trials such as STEP 1 and SURMOUNT-1 demonstrating clinically meaningful weight reduction (2,3). However, the clinical value of these therapies increasingly depends on long-term continuation of therapy, cardiometabolic outcomes, and real-world implementation. Maintenance studies show that discontinuation is associated with weight regain and worsening of metabolic and functional measures, while continued therapy helps sustain improvements linked to reduced obesity-related complications (6-8) . Real-world evidence highlights discontinuation, lower-than-trial dosing, access barriers, and follow-up challenges that may limit translation of trial efficacy into routine care (9,10). This narrative review examines landmark efficacy trials, maintenance and withdrawal data, real-world evidence, and selected future therapies, including retatrutide, orforglipron, and CagriSema. For family physicians, the key implication is that obesity pharmacotherapy should be approached as individualized, long-term chronic disease care aimed not only at weight reduction, but also at sustaining cardiometabolic health, function, and quality of life.

Keywords: Obesity; pharmacotherapy; GLP-1 receptor agonists; tirzepatide; semaglutide; primary care; family medicine; weight maintenance