



Obesity Treatment

“Obesity is a chronic disease requiring enhanced research, treatment, and prevention efforts.”

— *The Canadian Medical Association*

Insights from Dr. Lee Kaplan, MD, PhD






Dr. Lee Kaplan is an obesity medicine specialist whose work focuses on the development of new and more effective strategies for the prevention and treatment of obesity. He notes that:

“Overeating does not cause obesity; obesity causes overeating.”¹



Pharmacotherapy options in Canada*2,3

Product	Orlistat (Xenical®) ⁴	Liraglutide (Saxenda®) ⁵	Naltrexone/bupropion (Contrave®) ⁶
Drug class	Gastrointestinal lipase inhibitor	GLP-1 receptor agonist	Opioid antagonist/ NDRI
Mode of administration	Oral 	Subcutaneous 	Oral 
Dosing/titration	120 mg, TID [†]	Dose escalation for 5 weeks, once daily: Week 1: 0.6 mg Week 2: 1.2 mg Week 3: 1.8 mg Week 4: 2.4 mg Week 5: 3.0 mg (maintenance dose) [‡]	Dose escalation for 4 weeks: Week 1: • 8 mg/90 mg (1 tablet), once daily, AM Week 2: • 8 mg/90 mg (1 tablet), twice daily, AM and PM Week 3: • 16 mg/180 mg (2 tablets), AM • 8 mg/90 mg (1 tablet), PM Week 4: • 16 mg/180 mg (2 tablets), BID, AM and PM (maintenance dose) [‡]
% weight loss at 1 year[†]	-2.9%	-5.4%	-4.8%
Weight change over longer term[†]	-2.8 kg at 4 years	-4.2% at 3 years	Not studied
Effect on prediabetes[§]	37.3% reduction in risk of developing T2DM over 4 years	79% reduction in risk of developing T2DM over 3 years	Not studied
Contraindications	<ul style="list-style-type: none"> • Cholestasis • Chronic malabsorption syndrome • Pregnancy 	<ul style="list-style-type: none"> • Past history of pancreatitis • Personal or family history of medullary thyroid cancer • Personal history of MEN2 syndrome • Pregnancy 	<ul style="list-style-type: none"> • Uncontrolled hypertension • Any opioid use • History of or risk factors for seizures • Undergoing abrupt discontinuation of alcohol • Concomitant administration of MAOIs • Severe hepatic impairment • End-stage renal failure • Pregnancy
Common side effects	<ul style="list-style-type: none"> • Loose, oily stools • Flatus 	<ul style="list-style-type: none"> • Nausea • Constipation • Diarrhea • Vomiting 	<ul style="list-style-type: none"> • Nausea • Constipation • Headache • Dry mouth • Dizziness • Diarrhea
Other considerations	<ul style="list-style-type: none"> • Liver failure • Nephrolithiasis • Acute kidney injury • Fat-soluble vitamins • Levothyroxine • Cyclosporine • Oral anticoagulants • Anticonvulsants 	<ul style="list-style-type: none"> • Pancreatitis • Cholelithiasis • May affect absorption of medications due to slowing of gastric emptying 	<ul style="list-style-type: none"> • Seizure • Worsening of depression • Medications metabolized by CYP2D6 • Tamoxifen • CYP2B6 inhibitors • CYP2B6 inducers • Dopaminergic drugs

Adapted from Pedersen, et al.³
* Please refer to the respective Product Monographs for full dosing information.
† Assess after 3 months.
‡ Placebo subtracted.

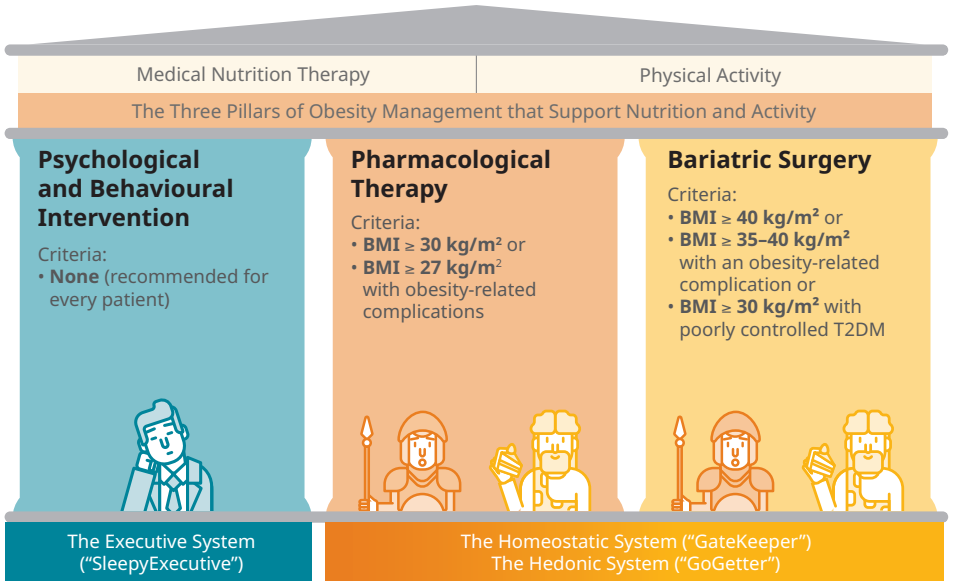
BID, twice a day; MAOI, monoamine oxidase inhibitor; MEN2, multiple endocrine neoplasia syndrome; NDRI, norepinephrine-dopamine reuptake inhibitor; T2DM, type 2 diabetes mellitus; TID, three times a day.

§ Health Canada has not approved Xenical®, Saxenda®, and Contrave® for use in the treatment of T2DM.

Canadian guidelines for the clinical management of obesity^{2,7-18}

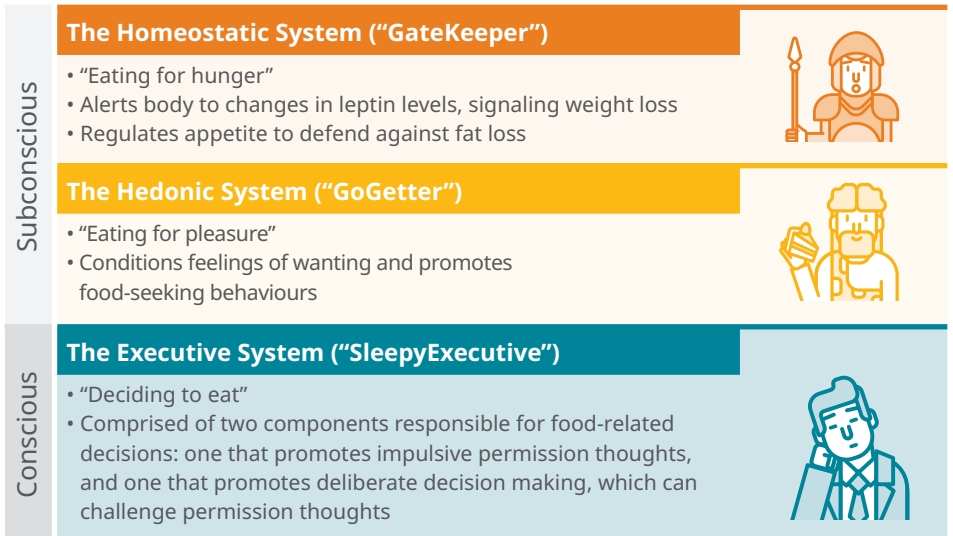
Treatment should be individualized to meet the needs of your patients, and it must address the common causes of weight regain to promote long-term weight maintenance.

Advise patients of all obesity treatment options

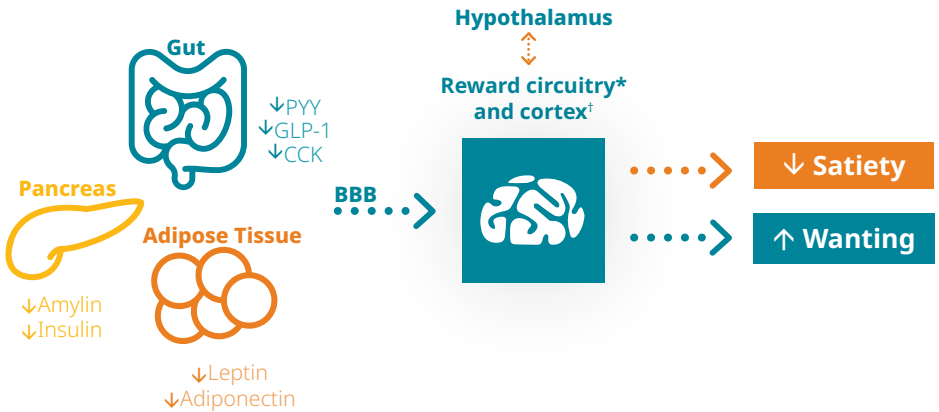
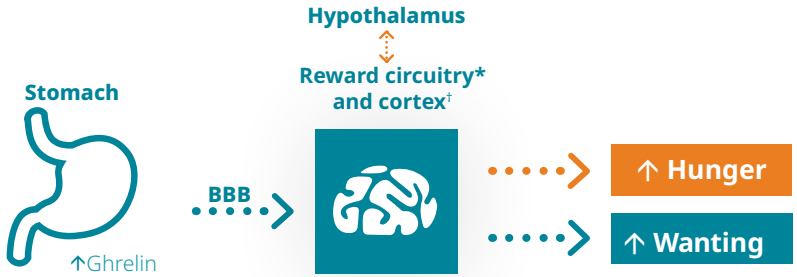


BMI, body mass index; T2DM, type 2 diabetes mellitus.

The appetite system



Why are weight loss and weight maintenance difficult?^{7,19}



Insights from Dr. David Macklin, MD, CCFP









Dr. David Macklin is a University of Toronto-trained family physician/GP psychotherapist who has been in practice treating obesity for the past 15 years. He states the following:

“Obesity is a **real medical condition** that is mostly genetic, centered in the brain, strongly influenced by the environment, and progressive.”

* The brain's reward circuitry, especially in the ventral tegmental area and nucleus accumbens.
† In particular, the dorsolateral pre-frontal cortex.
BBB, blood-brain barrier; CCK, cholecystokinin; GLP-1, glucagon-like peptide-1; PYY, peptide YY.

Why do medications work?²⁰⁻²³

There are biological limits to what an individual living with obesity can do. In response to weight loss, the body defends against further weight loss through compensatory mechanisms. Anti-obesity medications are tools that can help in mitigating these biological responses.

After weight loss, the body responds with:	Anti-obesity medications work by:
 <p>Increased physical hunger signals</p>	 <p>Helping patients stick to their calorie deficit</p>
 <p>Greater sensitivity to food rewards</p>	 <p>Reducing the heightened appetite and cravings in response to weight loss</p>
 <p>Slowing of metabolism</p>	 <p>Preventing weight re-gain</p>

Weight management requires a comprehensive approach, tailored to meet a patient's needs. Treatment is available in the form of psychological interventions, medications, and surgery, and these can all play a role in weight management.

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