Pharmacotherapy for obesity management

- **Pharmacotherapy should be considered as an adjunct to medical nutrition therapy, physical activity and psychological interventions.**
- Goals of pharmacotherapy should include the concept of best weight, the weight a person can achieve and maintain while living their healthiest and happiest life.
- The need for long-term treatment should be reviewed with the patient to ensure a comprehensive, shared approach to therapy selection is provided.
- Follow-up should focus on incremental, personalized behaviour changes that align with the individual's core values, with healthcare.

Pharmacotherapy options below are recommended for adults with:

- BMI of 30 kg/m² or greater
- BMI of 27 kg/m² or greater with at least one adiposity-related complication (e.g., HTN, T2DM, dyslipidemia)

Body Mass Index (BMI) does not directly measure body fat or health risks, fails to account for body fat distribution or muscle mass, and is less accurate for various populations such as women, ethnic minorities, and those with disabilities.

Benefits of pharmacotherapy typically require long-term treatment and may include:

- Weight loss
- Reduction in symptoms of adiposity-related comorbidities
- Improved quality of life (QoL)
- Prevention of weight regain
- Reduction in risk of cardiovascular disease (CVD)

Pharmacotherapy indicated for obesity management

Medication	Features (* = placebo subtracted)	Dosing and onset	Adverse drug reactions, warnings and contraindications	Cost and coverage (3-month supply)
Glucagon-like peptide-1 (GLP-1) receptor agonist ***Helps regulate appetite and reduce caloric intake, stimulates insulin secretion, and inhibits glucagon secretion in a glucose-dependent manner..***				
liraglutide (Saxenda®) 0.6mg, 1.2mg, 1.8mg, 2.4mg, 3mg/dose Pre-filled pen (multi-use)	**Weight loss (%)*:** ↓ 5.4% at 1 year and ↓ 4.2% at 3 years ≥ 5% ↓ at 1 year*: 36.1% ≥ 10% ↓ at 1 year*: 22.5% **A1c***: ↓ 1% at 1 year **CVD outcomes**: ↓ MACE and ↓ CV death HR*: ↑ 2.4 bpm BP*: ↓ 2.87 mmHg SBP ↓ 0.73 mmHg DBP **May be preferred for patients with**: • Abnormal satiety (hungry gut) • Cravings • Prediabetes and type 2 diabetes • Dyslipidemia • Hypertension • Obstructive sleep apnea (BMI > 30 kg/m²) • MASLD	**Initial:** 0.6mg subcut daily **Titration:** ↑ by 0.6mg every week to target a dose of 1.2, 1.8, 2.4 or 3mg subcut once daily **Target:** 3mg subcut daily **Onset:** 2 weeks **Plateau:** 34-40 weeks **Renal:** No adjustment necessary in CKD, however ↑ side effects (fatigue, GI). Not recommended in ESRD (eGFR < 15 mL/min) **Hepatic:** Not recommended for patients with hepatic impairment	**Side effects:** **CNS:** headache, dizziness, fatigue **GI:** nausea, vomiting, diarrhea, constipation, abdominal pain, dyspepsia **CV:** ↑ heart rate **Warnings:** • Risk of thyroid cancer • ↑ heart rate, caution in conditions that may worsen with increased HR (tachyarrhythmias) • Hypoglycemia risk with insulin or sulfonylureas • Intestinal obstruction and ileus • Cholelithiasis and pancreatitis **Contraindications:** • Personal or family history of medullary thyroid cancer • Personal history of MEN 2 • Pregnancy, breastfeeding (stop 2 months before pregnancy) **Interactions:** May affect absorption of medications due to delayed gastric emptying.	$1250-1500 **ODB**: X **NIHB**: X

Medication	Features (* = placebo subtracted)	Dosing and onset	Adverse drug reactions, warnings and contraindications	Cost and coverage (3-month supply)
Glucagon-like peptide-1 (GLP-1) receptor agonist *Helps regulate appetite and reduce caloric intake, stimulates insulin secretion, and inhibits glucagon secretion in a glucose-dependent manner.*				
semaglutide (Wegovy®) 0.25mg, 0.5mg, 1mg, 1.7mg, 2.4mg/dose Pre-filled (multi-dose) and single-dose pens	**Weight loss (%)*:** ↓ 12.5% at 1 year, not studied long-term ≥ 5% ↓ at 1 year*: 54.9% ≥ 10% ↓ at 1 year*: 57.1% **A1c*:** ↓ 1.2% at 1 year HR*: ↑ 4.2 bpm BP*: ↓ 5.1 mmHg SBP ↓ 2.4 mmHg DBP **CVD outcomes:** ↓ MACE and ↓ CV death **May be preferred for patients with:** • Abnormal satiety (hungry gut) • Cravings • Prediabetes and type 2 diabetes • Dyslipidemia • Hypertension • MASLD	**Initial:** 0.25mg subcut once weekly x 4 weeks **Titration:** ↑ every 4 weeks to target a dose of 0.5, 1, 1.7 or 2.4mg subcut once weekly **Target:** 2.4mg subcut once weekly **Onset:** 4 weeks **Plateau:** 52-60 weeks **Renal:** No adjustment necessary in CKD, not recommended in ESRD (eGFR < 15 mL/min) **Hepatic:** Not studied. Use with caution in hepatic impairment	**Side effects:** **CNS:** headache, dizziness, fatigue **GI:** nausea, vomiting, diarrhea, constipation, abdominal pain, dyspepsia **CV:** ↑ heart rate **Warnings:** • Risk of thyroid cancer • ↑ heart rate, caution in conditions that may worsen with increased HR (tachyarrhythmias) • Hypoglycemia risk with insulin or sulfonylureas. • Intestinal obstruction and ileus • Cholelithiasis and pancreatitis • Diabetic retinopathy **Contraindications:** • Personal or family history of medullary thyroid cancer • Personal history of MENS 2 • Pregnancy, breastfeeding (stop 2 months before pregnancy) **Interactions:** May affect absorption of medications due to delayed gastric emptying.	$1250-1500 **ODB**: X **NIHB**: X

Medication	Features (* = placebo subtracted)	Dosing and onset	Adverse drug reactions, warnings and contraindications	Cost and coverage (3-month supply)
Opioid receptor antagonist - Norepinephrine and dopamine reuptake inhibitor *Affects the regulation of food intake in the hypothalamus (appetite regulatory centre) and mesolimbic dopamine circuit (reward system).*				
naltrexone-bupropion (Contrave®) 8mg/90mg extended-release tablets	**Weight loss (%)*:** ↓ 4.8% at 1 year, not studied long-term ≥ 5% ↓ at 1 year*: 32% ≥ 10% ↓ at 1 year*: 18% **A1c*:** ↓ 0.5% at 1 year **CVD outcomes**: Trial ongoing (INFORMUS) HR*: ↑ 1.1 bpm **May be preferred for patients with**: • Cravings • Tobacco/nicotine dependence • Depression	**Initial:** 1 tablet in the morning daily **Titration:** ↑ by 1 tablet (8mg/90mg) every week until dose of 2 tablets in the morning and 2 tablets in the evening **Target:** 2 tablets twice daily **Onset:** 4 weeks **Plateau:** 28-36 weeks **Renal:** Moderate to severe impairment (eGFR 15-59 mL/min): 1 tablet in the morning and 1 tablet in the evening **Hepatic:** Mild to moderate impairment (Child-Pugh A & B): 1 tablet in the morning Severe impairment (Child-Pugh C): Contraindicated	**Side effects:** **CNS:** headache, sleep disturbance, nervousness, dizziness, fatigue **GI:** nausea, vomiting, diarrhea, **Anticholinergic**: dry mouth, constipation, blurred vision **CV:** ↑ blood pressure, ↑ heart rate **Warnings:** • Behavioural and emotional changes • Interference with opioid containing medications **Contraindications:** • Concomitant use of MAOI inhibitors • Uncontrolled hypertension • Current or history of seizure disorder • Use with other bupropion products • Abrupt d/c of alcohol, benzodiazepines or other sedatives and antiepileptic drugs • Chronic opioid use • Pregnancy, breastfeeding • Severe hepatic impairment (Child-Pugh score C) • ESRD **Interactions:** ↓ dose may be needed for CYP 2D6 substrates such as SSRIs, venlafaxine, TCAs, beta-blockers, and Type 1c antiarrhythmic agents. Avoid use with tamoxifen. Contraindicated with other bupropion products and chronic opioid use as it may block opioid effects. Avoid with high fat meals as it can increase absorption.	$750-1000 **ODB**: X **NIHB**: X

Medication	Features (* = placebo subtracted)	Dosing and onset	Adverse drug reactions, warnings and contraindications	Cost and coverage (3-month supply)
Gastrointestinal lipase inhibitor *Inhibits the enzyme lipase in the lumen of the stomach and small intestine which reduces the absorption of dietary fats, resulting in decreased caloric intake and weight loss.*				
orlistat (Xenical®) 120mg capsule	**Weight loss (%)*:** ↓ 2.9% at 1 year and ↓ 2.8% at 4 years ≥ 5% ↓ at 1 year*: 21% ≥ 10% ↓ at 1 year*: 12% **A1c***: ↓ 0.4% at 1 year **CVD outcomes**: Not studied HR*: ↔ no change BP*: ↓ 1.7 mmHg SBP ↓ 0.71 mmHg DBP **May be preferred for patients with**: • Income insecurity	**Initial:** 1 capsule TID with fatty meal (up to 1 hour after meal) **Titration:** Not required **Max:** 120mg TID with meals If a meal is missed or contains no fat, the dose may be omitted. **Onset:** 2 weeks **Plateau:** 16 - 20 weeks **Renal:** Not studied; post-marketing reports of renal failure **Hepatic:** Not studied; post-marketing reports of hepatic failure	**Side effects:** **GI:** oily spotting and loose stools, flatus with discharge, fecal urgency and increased defecation **CV:** slight ↓ in BP, no change in HR **Warnings:** • Use with caution in pre-existing disease of the large bowel or rectum • Liver failure • Kidney stones **Contraindications:** • Cholestasis • Chronic malabsorption syndrome • Pregnancy, breastfeeding **Interactions:** May affect absorption of fat-soluble vitamins and medications such as levothyroxine, cyclosporin, oral anti-coagulants and anti-convulsants. In cases of severe diarrhea, use a backup contraceptive method. Recommended to take a multivitamin daily.	$500-650 **ODB**: X **NIHB**: X
Glucagon-like peptide-1 (GLP-1) receptor agonist and gastric inhibitory polypeptide (GIP) *Regulates appetite and caloric intake, stimulates insulin secretion, and inhibits glucagon secretion in a glucose-dependent manner.*				
tirzepatide (Zepbound®) 2.5mg, 5mg, 7.5mg, 10mg, 12.5mg, 15mg/dose In pre-filled pens or single-dose vials **Currently not available or approved for obesity in Canada**	**Weight loss (%)*+:** ↓ 12 – 18% at 72 weeks, not studied long term ≥ 5% ↓ at 72 weeks*+: 50.6 – 56.4% ≥ 10% ↓ at 72 weeks*+: 49.7 – 64.7% **A1c*+**: ↓ 0.4 – 0.51% at 72 weeks **CVD outcomes:** Trial ongoing (SURMOUNT-MMO) HR*: 1-3 bpm BP*: ↓ 6.2 mmHg SBP ↓ 4 mmHg DBP **May be preferred for patients with**: • Abnormal satiety (hungry gut) • Type 2 diabetes • Dyslipidemia • Hypertension • Obstructive sleep apnea (BMI > 30 kg/m^2) + 5, 10 and 15mg results reported	**Initial:** 2.5mg subcut once weekly x 4 weeks **Titration:** ↑ by 2.5mg every 4 weeks to target a dose of 5, 10 or 15mg subcut once weekly **Target:** 5, 10 or 15mg subcut once weekly **Onset:** 4 weeks **Plateau:** 60-72 weeks **Renal:** No adjustment necessary in CKD, not recommended in ESRD (eGFR < 15 mL/min) **Hepatic:** Use with caution in hepatic impairment	**Side effects:** **CNS:** headache, sleep disturbance, nervousness, dizziness, fatigue **GI:** nausea, vomiting, diarrhea **CV:** ↑ heart rate **Warnings:** • Risk of thyroid cancer • Caution in heart conditions that may worsen with increased HR (tachyarrhythmias) • Hypoglycemia risk with insulin or sulfonylureas. • Intestinal obstruction and ileus • Cholelithiasis and pancreatitis • Diabetic retinopathy • Risk of malnutrition **Contraindications:** • Personal or family history of medullary thyroid cancer • Personal history of MENS 2 • Pregnancy, breastfeeding (stop 2 months before pregnancy) **Interactions:** May affect absorption of medications due to delayed gastric emptying. If taking oral contraceptives, switch to non-oral contraceptive method or add a barrier method for 4 weeks after initiation and each dose escalation.	Currently not available

Pharmacotherapy indicated for type 2 diabetes (with obesity management benefits)

Medication	Features (* = placebo subtracted)	Dosing and onset	Adverse drug reactions, warnings and contraindications	Cost and coverage (3-month supply)
Glucagon-like peptide-1 (GLP-1) receptor agonist *Helps regulate appetite and reduce caloric intake, stimulates insulin secretion, and inhibits glucagon secretion in a glucose-dependent manner.*				
liraglutide (Victoza®) 0.6mg, 1.2mg, 1.8mg/ dose Pre-filled pen (multi-use)	**Weight loss*:** ↓ 2.3kg at 36 weeks **A1c*:** ↓ 0.4% at 36 weeks **CVD outcomes:** ↓ MACE and ↓ CV death HR*: ↑ 3 bpm BP*: ↓ 1.2 mmHg SBP ↑ 0.6 mmHg DBP	**Initial:** 0.6mg subcut daily **Titration:** ↑ by 0.6mg every week to target a dose of 1.2 or 1.8mg subcut once daily **Max:** 1.8mg subcut daily **Onset:** 2 weeks **Plateau:** 34-40 weeks **Renal:** No adjustment necessary in CKD, not recommended in ESRD (eGFR < 15 mL/min) **Hepatic:** No adjustment in hepatic impairment	Refer to Saxenda® above for more information	$1000-1250 **ODB**: X **NIHB**: X
semaglutide (Ozempic®) 0.25mg, 0.5mg, 1mg/ dose Pre-filled pen (multi-use)	**Weight loss*:** ↓ 2.3kg at 36 weeks **A1c*:** ↓ 0.4% at 36 weeks **CVD outcomes:** ↓ MACE and ↓ CV death HR*: ↑ 3 bpm BP*: ↓ 1.2 mmHg SBP ↑ 0.6 mmHg DBP	**Initial:** 0.25mg subcut once weekly **Titration:** ↑ every 4 weeks to target a dose of 0.5, 1 or 2mg subcut once weekly **Max:** 2mg subcut once weekly **Onset:** 4 weeks **Plateau**: 52-60 weeks **Renal:** No adjustment necessary in CKD, not recommended in ESRD (eGFR < 15 mL/min) **Hepatic:** Not studied. Use with caution in hepatic impairment	Refer to Wegovy® above for more information	$750-1000 (at 1mg dose) $1500 (at 2mg dose) **ODB**: ✓ LU 665, 667 (T2DM + metformin failed or contraindicated) **NIHB**: ✓
semaglutide (Rybelsus®) 3mg, 7mg, 14mg Oral tablets	**Weight loss*:** ↓ 2.6-3.8kg at 1 year **A1c*:** ↓ 0.9-1.2% at 1 year **CVD outcomes**: Non-inferior to placebo for MACE and CV death. Did not reach statistical significance for superiority for MACE. HR*: ↑ 1 – 3 bpm BP*: ↔ no change	**Initial:** 3mg PO once daily for 30 days **Titration:** ↑ to 7mg PO daily for 30 days. Then can stay or ↑ 14mg PO daily. **Max:** 14mg PO once daily **Onset:** < 12 weeks **Plateau:** 30-36 weeks **Hepatic:** No adjustment in CKD **Renal:** Post-marketing reports of acute renal failure and worsening CKD. Safety and efficacy established in moderate CKD (eGFR 30 to 59mL/ min).	Refer to Wegovy® above for more information	$750-999 **ODB**: ✓ LU 662,663,664 (T2DM + met-formin failed or contraindicated) **NIHB**: ✓ LU (in addition to other antihyperglyce-mics)

Medication	Features (* = placebo subtracted)	Dosing and onset	Adverse drug reactions, warnings and contraindications	Cost and coverage (3-month supply)
Glucagon-like peptide-1 (GLP-1) receptor agonist and gastric inhibitory polypeptide (GIP) *Regulates appetite and caloric intake, stimulates insulin secretion, and inhibits glucagon secretion in a glucose-dependent manner.*				
tirzepatide (Mounjaro®) 2.5mg, 5mg, 7.5mg, 10mg, 12.5mg, 15mg/ dose **Pre-filled pen (multi-use) currently not available in Canada**	**Weight loss (%)*+:** ↓ 5.3-6.8kg at 40 weeks **A1c*+**: ↓ 1.55 - 2.03% **CVD outcomes:** Trial ongoing (SURPASS-CVOT) HR*: ↑ 1.3 – 3.3 bpm BP*: ↓ 4-7 mmHg SBP ↓1-2 mmHg DBP + 5, 10 and 15mg results reported	Refer to Zepbound® above for more information	Refer to Zepbound® above for more information	$1000-1250 **ODB**: X **NIHB**: X

* Placebo subtracted – placebo ranged from 7-33% depending on the medication and amount of weight loss

Legend:
BP = blood pressure; CNS = central nervous system; CV = cardiovascular; CVD = cardiovascular disease; DBP = diastolic blood pressure; ESRD = end-stage renal disease; GI = gastrointestinal; HR = heart rate; HTN = hypertension; MAOI = monoamine oxidase inhibitors; MEN 2 = multiple endocrine neoplasia syndrome type 2; MACE = major-adverse cardiovascular event; MASLD = metabolic dysfunction-associated steatotic liver disease; SBP = systolic blood pressure; T2DM = type 2 diabetes mellitus

Combination of anti-obesity drug therapy has limited data to support use.

Coverage is a barrier to access. Individuals may need to self-advocate with their employer to gain access to pharmacotherapy.

Drug cost is an approximate range for a 3-month supply (including mark-up of 10% and dispensing fee of $12.99) at the target dose.

Follow-up may be more frequent during the titration phase to monitor the efficacy and safety of the chosen treatment. Once a patient is stabilized, follow-up appointments can occur at regular points up to the clinician's discretion.

Onset is the time at which weight-loss begins to occur.

Plateau is the time at which the weight-loss begins to level-off.

Titration protocols can be completed at a slower pace than outlined above based on clinician discretion and patient tolerability/satisfaction.