In the name of God

Canadian Adult Obesity Clinical Practice Guideline

obesity canada obésité canada

Pharmacotherapy for obesity management in adults

2025 clinical practice guideline update

Sue D. Pedersen MD, FRCPC, DABOM[i], Priya Manjoo MD, MSc, FRCPC, DABOM, CHS, [ii], Satya Dash MD, FRCPC[iii], Akshay Jain, MD, FRCPC, FACE, CCD, ECNU, DABOM[iv], Nicole Pearce, PMC, CPC(HC)[v], Megha Poddar, MD, FRCPC, DABOM[vi]

i. C-ENDO Diabetes & Endocrinology Clinic, and University of Calgary, Calgary, Alberta
ii. Department of Endocrinology, University of British Columbia & University of Victoria, Victoria, British Columbia
iii. Department of Medicine University of Toronto & University Health Network, Toronto, Ontario
iv. Dept of Endocrinology, University of British Columbia, TLC Diabetes and Endocrinology Clinic, Surrey, British Columbia
v. Obesity Canada, Edmonton, Alberta
vi. Department of Internal Medicine, McMaster University, Hamilton, Ontario

Cite this Chapter

Pedersen SD, Majoo P, Dash S, Jain A, Pearce N, Poddar M. Canadian Adult Obesity Clinical Practice Guideline: Pharmacotherapy for Obesity Management in Adults. Available from: obesitycanada.ca/healthcare-professionals/adult-clinical-practice-guideline. Accessed [date].

Update History

Version 3, August 11, 2025. Adult Obesity Clinical Practice Guideline are a living document.

سروناز فروزنده

Scope:

In this guideline, we inform on the use of pharmacotherapy for management of obesity and weight-related health complications in adults aged 18 years and older.

Assessment:

Body mass index (BMI) does not provide information on body composition or fat distribution. The anthropometric measures noted in recommendation 1 (Table 1) correlate strongly with adiposity-related complications and vary by sex and ethnicity.

Initiating pharmacotherapy:

- The patient and health care professional should work together to identify clear goals of therapy before initiating obesity pharmacotherapy, including a discussion about reasonable Expectations of treatment, and potential benefits versus risks of Pharmacotherapy (Table 1, recommendation 2)

- In addition to weight loss, treatment targets may include:

1. reduction in cardiometabolic risk
2. improvement, remission of adiposity-related complications
3. maintenance of weight loss
4. management of appetite or cravings
5. improvement in quality of life

Table 2 defines the levels of evidence and grades of recommendations.

Table 2: Classification of evidence and recommendations*

Levels of evidence	
1A	Evidence from at least 1 meta-analysis of RCTs or individual RCT
2A	Evidence from at least 1 controlled study without randomization
2B	Evidence from at least 1 other type of quasi-experimental study
3	Evidence from nonexperimental descriptive studies, such as comparative studies, correlation studies, and case–control studies
4	Evidence from expert committee reports or opinions or clinical experience of respected authorities, or both
Grades of recommendations	
A	Directly based on level I evidence
B	Directly based on level II evidence or extrapolated from level I evidence
C	Directly based on level III evidence or extrapolated from level I or II evidence
D	Directly based on level IV evidence or extrapolated from level I, II, or III evidence

RCT = randomized controlled trial.

*Note: Levels of evidence and grades of recommendations adapted with permission from BMJ Publishing Group Limited. Shekelle PG, Woolf SH, Eccles M, et al. Developing guidelines. *BMJ* 1999;318:593-6.[48] Large multinational RCTs are now directly classified as level 1a evidence, reflecting their high methodological quality and broad applicability. This change explains the lack of a row for level 1B evidence in this table. For a detailed description of the full methodology and the process of downgrading studies to lower levels of evidence, please refer to the 2020 Canadian adult obesity clinical practice guideline.[8]

Recommendations:

We developed 13 recommendations (Table 1) to guide clinicians on the selection, initiation, and long-term use of obesity pharmacotherapy.

Table 1 (part 1 of 2): Recommendations on pharmacotherapy for the management of obesity in adults

No.	Recommendation	Category of evidence; strength of recommendation
1.	We recommend the use of measures of central adiposity (using sex- and ethnicity-specific cut-offs if applicable), such as waist circumference, waist-to-hip ratio, or waist-to-height ratio, in addition to ethnicity-specific BMI thresholds or adiposity-related complications, to guide the decision to initiate pharmacotherapy.[14–17]	Level 3; grade C
2.	We suggest that the initiation of obesity pharmacotherapy, in conjunction with health behaviour changes, for adults with excess adiposity be personalized to meet individual values, preferences, and treatment goals to support an approach that is safe, effective, culturally acceptable, and affordable for long-term adherence.	Level 4; grade D consensus

3.	Pharmacotherapy for obesity management, in conjunction with health behaviour changes, should be offered to people with BMI ≥ 30,* or BMI ≥ 27* with adiposity-related complications: • Semaglutide 2.4 mg weekly (BMI ≥ 27*) (level 1a; grade A)[18] • Tirzepatide 5 mg, 10 mg, or 15 mg weekly (BMI ≥ 27*) (level 1a; grade A)[19] • Liraglutide 3 mg daily (BMI ≥ 27*) (level 2a; grade B)[20] • Naltrexone–bupropion 16 mg/180 mg twice daily (BMI 27–45*) (level 2a; grade B)[21] • Orlistat 120 mg 3 times daily (BMI 28–47*) (level 2a; grade B)[22] *See recommendation 1.	See recommendation

4.	Pharmacotherapy for obesity management, in conjunction with health behaviour changes, should be used long term, when effective, to:
	• Avoid weight regain and regression of health benefits achieved with pharmacotherapy:
	  • Semaglutide 2.4 mg weekly (level 1a; grade A)[23]
	  • Tirzepatide 10 mg or 15 mg weekly (level 1a; grade A)[24]
	  • Orlistat 120 mg 3 times daily (level 2a; grade B)[22]
	• Maintain weight loss and prevent weight regain following health behaviour changes alone:
	  • Liraglutide 3 mg daily (level 2a; grade B)[25]
	  • Orlistat 120 mg 3 times daily (level 2a; grade B)[26]
	  • Tirzepatide 10 mg or 15 mg (level 2a; grade B)[27]
		See recommendation

5.	Pharmacotherapy should be offered, in conjunction with health behaviour changes, to reduce the occurrence of major adverse cardiovascular events in people with established ASCVD and BMI ≥ 27,* in addition to standard of care for ASCVD: • Semaglutide 2.4 mg weekly[28] *See recommendation 1.	Level 2a; grade B

6.	Pharmacotherapy should be offered, in conjunction with health behaviour changes, to people living with heart failure with preserved ejection fraction and BMI ≥ 30,* in addition to standard of care, for weight loss and:
	• A composite of reduction in cardiovascular death or a worsening heart failure event:
	  • Tirzepatide 15 mg weekly[29]
	• Improvement in heart failure symptoms:
	  • Semaglutide 2.4 mg weekly[30]
	  • Tirzepatide 15 mg weekly[29]
	*See recommendation 1.
		Level 1a; grade A

7.	Obesity pharmacotherapy, in conjunction with health behaviour changes, for people living with prediabetes should be offered for weight loss and to:
	• Reduce the risk of progression to type 2 diabetes:
	  • Liraglutide 3 mg daily (BMI ≥ 27*) (level 2a; grade B)[31]
	  • Orlistat 120 mg 3 times daily (BMI ≥ 30*) (level 2a; grade B)[32]
	  • Tirzepatide 5 mg, 10 mg, or 15 mg weekly (BMI ≥ 27*) (level 2a; grade B)[33]
	• Achieve normoglycemia:
	  • Semaglutide 2.4 mg weekly (BMI ≥ 30*) (level 1a; grade A)[34]
	*See recommendation 1.
		See recommendation

Table 1 (part 2 of 2): Recommendations on pharmacotherapy for the management of obesity in adults

No.	Recommendation	Category of evidence; strength of recommendation
8.	Obesity pharmacotherapy should be offered, in conjunction with health behaviour changes, to people living with type 2 diabetes for weight loss and improvement in glycemic control: • Semaglutide 2.4 mg weekly (BMI ≥ 27*) (level 1a; grade A)[35] • Tirzepatide 10 mg or 15 mg weekly (BMI ≥ 27*) (level 1a; grade A)[36] • Liraglutide 3 mg daily (BMI ≥ 27*) (level 2a; grade B)[37] • Naltrexone–bupropion 16 mg/180 mg twice daily (BMI 27–45*) (level 2a; grade B)[38] • Orlistat 120 mg 3 times daily (BMI 27–43*) (level 2a; grade B)[39] *See recommendation 1.	See recommendation

9.	Pharmacotherapy may be offered, in conjunction with health behaviour changes, in treating people living with MASH, for weight loss and:
	• Resolution of MASH without worsening of fibrosis:
	  • Semaglutide 2.4 mg weekly (level 2a; grade B)[40]
	  • Liraglutide 1.8 mg daily (BMI ≥ 25*) (level 3; grade C)[41]
	  • Tirzepatide 5 mg, 10 mg, or 15 mg weekly (BMI 27–50*) (level 3; grade C)[42]
	• Improvement in fibrosis without worsening of MASH:
	  • Semaglutide 2.4 mg weekly (level 2a; grade B)[40]
	  • Tirzepatide 5 mg, 10 mg, or 15 mg weekly (BMI 27–50*) (level 3; grade C)[42]
	*See recommendation 1.
		See recommendation

10.	Pharmacotherapy should be offered, in conjunction with health behaviour changes, for weight loss and improvement in apnea-hypopnea index in people who are living with moderate to severe obstructive sleep apnea and BMI ≥ 30,* and who are:
	• Unwilling or unable to use positive airway pressure therapy:
	  • Tirzepatide 10 mg or 15 mg (level 1a; grade A)[43]
	  • Liraglutide 3 mg daily (level 2a; grade B)[44]
	• Using positive airway pressure therapy:
	  • Tirzepatide 10 mg or 15 mg (level 1a; grade A)[43]
	*See recommendation 1.
		See recommendation

11.	Pharmacotherapy for obesity management should be offered, in conjunction with health behaviour changes, for people living with knee osteoarthritis and BMI ≥ 30* for weight loss and reduction in knee pain: • Semaglutide 2.4 mg weekly[45] *See recommendation 1.	Level 1a; grade A

12.	Setmelanotide up to 3 mg daily may be offered for weight management for people with BMI ≥ 30* and: • Bardet–Biedl syndrome (level 2a; grade B)[46] • Genetically confirmed biallelic pro-opiomelanocortin, proprotein convertase subtilisin/kexin type 1, or leptin receptor deficiency due to variants interpreted as pathogenic, likely pathogenic, or of uncertain significance (level 3; grade C)[47] *See recommendation 1.	See recommendation

آگونیست گیرنده ملانوکورتین ٤ که مستقیما بر مسیر کنترل اشتها در مغز تاثیر می گذارد

13.	We recommend against the use of compounded medications, prescription medications, or over-the-counter medications other than those approved in Canada for weight loss in people with excess adiposity.	Level 4; grade D consensus

Semaglutide:

- Semaglutide is a once weekly, subcutaneously administered GLP-1RA that acts centrally on the pro-opiomelanocortin POMC/CART neurons
- reduce hunger
- reduce cravings
- slows gastric emptying
- indicated for long- term obesity management in adults at a dose of 2.4 mg weekly
- indicated for the treatment of obesity in pediatric patients age 12 and older

Titration Schedule:

- 0.25mg weekly x 4 weeks *then* 0.5mg weekly x 4 weeks *then*
- 1mg weekly x 4 weeks *then* 1.7mg weekly x 4 weeks *then*
- 2.4mg weekly

% of patients achieving ≥ 5% weight loss :

- 86.4% (vs 31.5% with placebo)

- In a randomized controlled trial (RCT) of 1961 people with BMI ≥ 30, or BMI ≥ 27 and at least 1 weight-related coexisting condition, without diabetes:
- semaglutide 2.4 mg weekly with health behaviour modification

resulted in a weight change of 14.9% at 68 weeks, compared with 2.4% with placebo.

adverse effects with semaglutide:

- transient, mild to moderate nausea, vomiting, and diarrhea, constipation, and heartburn leading to treatment discontinuation in 4.5% of participants versus 0.8% with placebo.
- occurred primarily during the dose-escalation period
- More gradual titration can help mitigate gastrointestinal side effects

- Rare adverse effects included gallbladder-related issues (mostly gallstones)
- 2.6% of the semaglutide group versus 1.2% with placebo.
- ileus and intestinal obstruction have been reported with semaglutide
- pancreatitis reported in 0.2% with semaglutide versus 0% with placebo

Contraindications :

- Personal or family history of medullary thyroid cancer
- Personal history of MEN2 syndrome
- Pregnancy, women attempting conception, breastfeeding

Pregnancy:

- The manufacturer recommends discontinuation of semaglutide at least two months before a planned pregnancy .

Tirzepatide:

- dual GIP/GLP1 receptor agonist
- The GLP-1 component acts centrally on the POMC/CART neurons
- improve satiation and satiety
- reduce hunger
- slows gastric emptying
- Like GLP-1, glucose-dependent insulinotropic polypeptide (GIP) is a nutrient-stimulated hormone that regulates energy balance through cell-surface receptor signaling in the brain and adipose tissue

- The recommended starting dose of tirzepatide is 2.5 mg weekly, with up-titration by 2.5 mg every 4 weeks as needed and tolerated to achieve the desired treatment goals, to a maximum dose of 15 mg weekly

% of patients achieving ≥ 5% weight loss:

- 85.1% (5mg)
- 88.9% (10mg)
- 90.9% (15mg)
- (vs 34.5% with placebo)

The most common adverse effects tirzepatide:

- mild to moderate gastrointestinal symptoms (nausea, diarrhea, constipation) during dose escalation
- More gradual titration can help mitigate gastrointestinal side effects

Rare adverse effects with tirzepatide:

- cholecystitis
- slightly more frequently (0.6%) than with placebo (0%)
- no increased risk of pancreatitis

Contraindication:

- personal or family history of medullary thyroid carcinoma
- patients with MEN 2 because of an increased risk of medullarythyroid
- Pregnancy, women attempting conception, breast-feeding

Pregnancy:

- For patients using oral contraceptives, it is recommended to switch to a non-oral contraceptive method, or to add a barrier method of contraception for 4 weeks after initiation and for 4 weeks after each dose escalation

- discontinuation of tirzepatide at least one month before a planned pregnancy

Liraglutide:

- Liraglutide is a daily, subcutaneously administered human glucagon-like peptide 1 (GLP-1) analog
- acts centrally on the pro-opiomelanocortin (POMC) and cocaine- and amphetamine-regulated transcript (CART) neurons in hypothalamus
- improve satiety
- reduce slows gastric emptying.
- indicated for the treatment of obesity in pediatric patients age 12 and older

Titration Schedule:

- 0.6mg daily x 1 week
- *then* 1.2mg daily x 1 week
- *then* 1.8mg daily x 1 week
- *then* 2.4mg daily x 1 week
- *then* 3.0 mg daily

% of patients achieving ≥ 5% weight loss :

- 63.2% (vs. 27.1% with placebo)

- In an RCT of 3731 people with BMI ≥ 30, or BMI ≥ 27 with untreated dyslipidemia or hypertension, but without diabetes, liraglutide 3 mg daily with health behaviour modification resulted in weight change of 8.0% ,2.6% with placebo at 56 weeks

The most common adverse effects with liraglutide:

- mild to moderate nausea, diarrhea, and constipation, vomiting and/or dyspepsia.

- More gradual titration can help mitigate gastrointestinal side effects.

Rare adverse effects:

- gallstones, reported in 0.8% of the liraglutide group versus 0.4% with placebo,
- with pancreatitis reported in 0.4% of the liraglutide group and less than 0.1% with placebo.
- intestinal obstruction and ileus

Contraindication:

- Liraglutide is contraindicated in patients with:
- a personal or family history of medullary thyroid cancer
- a personal history of multiple endocrine neoplasia type 2 (MEN 2) because of an increased risk of medullary thyroid cancer
- Pregnancy, women attempting conception, breastfeeding

Naltrexone/Bupropion:

- Naltrexone/bupropion is a combination extended-release
- tablet containing two medications.
- Bupropion is an antidepressant that induces satiety centrally by enhancing production and release of α-melanocyte stimulating hormone (*α*-MSH) and β-endorphin from the POMC cells in the hypothalamus.
- Naltrexone is an opioid receptor antagonist that disrupts the auto-inhibitory effect of *B* endorphin on the POMC cells by blocking the μ-opioid receptors

- combined tablet containing 8 mg naltrexone and 90 mg bupropion,

Titration Schedule:

- 1 tablet daily x 1 week
- *then* 1 tablet BID x 1 week
- *then* 2 tablets in AM ,1 tablet in PM x 1 week
- *then* 2 tablets BID

combined tablet containing 8 mg naltrexone and 90 mg bupropion

% of patients achieving ≥ 5% weight loss :

- 48% (vs. 16% with placebo)

- In an RCT of 1742 patients with BMI 30–45, or BMI 27–45 with dyslipidemia or hypertension, but without diabetes, naltrexone–bupropion 16 mg/180 mg twice daily with health behaviour changes was associated with weight change of 6.1% versus –1.3% with placebo at 56 weeks

The most common adverse effects with naltrexone–bupropion:

- nausea,headache, constipation, dizziness, vomiting, insomnia dizziness and dry mouth.Discontinuation because of adverse events was more commonin the naltrexone–bupropion group than in the placebo group(20.1% v. 9.6%)

Contraindication:

- Uncontrolled hypertension
- Any opioid use . Opioid therapy should be discontinued 7 to 10 days prior to initiation of naltrexone/bupropion to prevent the precipitation of opioid withdrawal.
- History of, or risk factors for, seizure
- Abrupt discontinuation of alcohol, benzodiazepines, barbiturates or antiepileptic drugs
- Concomitant administration of monoamine oxidase inhibitors (MAOI)
- Severe hepatic impairment
- End-stage renal failure
- anorexia nervosa, bulimia
- Pregnancy, women attempting conception, breastfeeding

drug interactions with naltrexone/bupropion :

- selective serotonin reuptake inhibitors, beta blockers, antipsychotic agents, type 1C antiarrhythmic agents and many tricyclic antidepressants, such as citalopram, metoprolol, risperidone, propafenone and desipramine, respectively

- naltrexone/ bupropion dosing should not exceed one tablet twice daily when used with CYP2B6 inhibitors (e.g., ticlopidine, clopidogrel)

Orlistat :

- inhibitor of pancreatic lipase
- inhibits the breakdown of dietary triglycerides into absorbable free fatty acids
- approximately 30% of ingested triglycerides are excreted, primarily in the feces, creating a caloric deficit.
- does not target appetite or satiety mechanisms
- indicated for the treatment of obesity in pediatric patients age 12 and older

Dose/frequency :

- 120 mg TID

- A meta-analysis of 16 RCTs of orlistat 120 mg 3 times daily (*n* = 10 631 participants) reported a mean placebo-subtracted weight change of 2.9% at 1 year

The most common adverse effects with orlistat:

- oily and loose stools, flatus
- with discharge, fecal urgency and increased defecation.
- fecal urgency, and spotting, occurring in 15%–30% of patients and leading to discontinuation in some cases
- interfere with the absorption of fat-soluble vitamins (A, D, E and K)
- Advice: patients should thus be counselled to take a multivitamin at least two hours before or after taking orlistat

The rare adverse effects:

- rare cases of severe liver injury or acute liver failure
- develop increased levels of urinary oxalate with orlistat; cases of
- oxalate nephropathy with renal failure

Contraindication:

- chronic malabsorption syndrome
- cholestasis

- **% of patients achieving ≥ 5% weight loss :**

54% (vs. 33% with placebo)

- interfere with vitamin K absorption, the international normalized ratio (INR) should be monitored closely
- affect absorption of levothyroxine and/or iodine salts; patients on levothyroxine should be monitored for changes in thyroid hormone levels
- reduce the availability of oral contraceptives
- reduction in plasma cyclosporine it is recommended to monitor cyclosporine levels
- affect absorption of anticonvulsants

Setmelanotide :

- melanocortin 4 receptor (MC4R) agonist
- restore impaired MC4R activity caused by extremely rare genetic deficits leading to hyperphagia and early onset severe obesity
- indicated for :
- Bardet-Biedl syndrome (BBS)
- genetically confirmed biallelic pro opiomelanocortin (POMC)
- proprotein convertase subtilisin/kexin type 1 (PCSK1)
- leptin receptor (LEPR) deficiency

- indicated for the treatment of these rare genetic conditions causing obesity in pediatric patients age 6 and olde

- starting dose of setmelanotide for adults is 1 mg daily, with titration by 0.5 mg every 2 weeks as tolerated to a maximum of 3 mg daily.

The most common side effects with setmelanotide :

- skin hyperpigmentation
- injection site reactions
- nausea and vomiting
- Spontaneous penile erections

Contraindication:

- personal or family history of melanoma or pre-melanoma skin lesions.
- pregnancy
- women attempting pregnancy
- breastfeeding

Atherosclerotic cardiovascular disease:

- Obesity is strongly associated with cardiovascular risk factors
- a major driver of atherosclerotic cardiovascular disease
- leading cause of morbidity and mortality worldwide

Heart failure with reduced ejection fraction (HFrEF) :

- Obesity may increase the risk of HFrEF based on some, but not all, data. Data are lacking to support that weight loss affects heart failure outcomes in people with obesity and HFrEF.

Prediabetes :

- Although the exact prevalence of prediabetes in people with obesity is not known, studies suggest that between 14.3% to 36.9% of adults with obesity may have prediabetes.

Type 2 diabetes :

- Obesity in people with T2D is associated with poorer glycemic control, blood pressure control and lipid profiles, as well as an increased use of lipid-lowering and antihypertensive medications, compared to those with T2D who do not have obesity.

Metabolic dysfunction-associated steatotic liver disease (MASLD) and metabolic dysfunction-associated steatohepatitis (MASH):

- MASLD (previously NAFLD) is the most prevalent chronic liver disease, affecting approximately 25% of adults globally.
- The spectrum of MASLD includes steatosis, metabolic dysfunction-associated steatohepatitis (MASH, previously NASH), fibrosis, and cirrhosis. MASLD is strongly associated with cardiometabolic risk factors, particularly T2D.

- In people living with obesity, the prevalence of MASLD has been estimated to be approximately 75%, and the prevalence of MASH about %34
- The management of MASLD is focused on weight loss in people with obesity

Obstructive sleep apnea :

- Obstructive sleep apnea (OSA) is a common, yet underdiagnosed chronic disorder characterized by obstructive apneas and hypopneas due to repetitive collapse of the upper airway during sleep, with excess weight being a leading risk factor. Weight reduction can reduce OSA severity and improve related health outcomes

Osteoarthritis :

- Obesity-related knee osteoarthritis is caused not only by increased weight stress on the joints, but also by the chronic inflammatory state that is seen in obesity.

- Managing weight effectively can significantly reduce knee pain, enhance physical function, and may slow osteoarthritis progression.

Polycystic ovary syndrome (PCOS) :

- Polycystic ovary syndrome is a common reproductive-endocrine disorder characterized by menstrual irregularities, elevated androgen levels and ovarian cysts affecting reproductive, metabolic and overall health.
- The prevalence of obesity is 3.8 times higher amongst individuals with PCOS than in those without PCOS.
- Weight loss is recommended for individuals with PCOS and obesity to improve cardiometabolic and reproductive health.
- Few, small studies have examined pharmacotherapy for weight management in individuals with PCOS.

Chronic kidney disease :

- Elevated BMI is associated with an increased risk of chronic kidney disease and kidney failure.
- Obesity has been recognized as an independent cause of CKD, termed obesity-related glomerulopathy

Gastroesophageal reflux disease (GERD) :

- GERD is common in people with obesity, and can improve with weight loss
- Onset of GERD, or exacerbation of pre-existing GERD, can occur with obesity

Mental health :

- The bidirectional relationship between obesity and mental health is complex
- Obesity is common in individuals with bipolar disorder
- Weight gain is a common side effect of some antipsychotic medication

Limitations :

- There are other medications (e.g., phentermine, phentermine/ topiramate) which are approved for the management of obesity in some countries. In these guidelines, we have included only those medications that are currently approved in Canada.

Thank you