

What is the role for orlistat (Xenical®) given the emergence of newer medications for weight loss in adults?

Conclusion: Orlistat (Xenical[®]) is the least effective of available weight loss medications with a weight loss effect of approximately 3 kg compared to placebo. Few people remain on orlistat long term and its gastrointestinal adverse event profile, dosing regimen and cost are disadvantages. It receives limited to no endorsement in clinical practice guidelines.

The BC Provincial Academic Detailing (PAD) service's topic <u>Medications for Weight Loss in Adults</u> looks at the evidence for tirzepatide, semaglutide, liraglutide, naltrexone-bupropion and orlistat.¹ Click to <u>book a session</u> with an academic detailing pharmacist in your area. Reviewing the evidence, we asked, **what is the role for orlistat (Xenical®)?**

- a) **Basics**: Orlistat (Xenical®) is approved by Health Canada for use in people with BMI ≥ 30 or BMI ≥ 27 with comorbidities.² It works non-systemically as a gastrointestinal lipase inhibitor, inhibiting the absorption of dietary fat. It can be taken up to three times a day with meals that contain fat (each dose: 120 mg). The annual cost is approximately \$2100 (excluding markup and professional fees).³ It is a non-benefit medication in B.C. Use the PharmaCare Formulary Search to review a list of non-benefit medications in B.C.⁴
- b) **Efficacy:** In a recent systematic review, compared to placebo, orlistat treatment resulted in 3% more weight loss (3 kg or 7 lbs, on average).⁵ The authors conclude that orlistat "possibly ranks no better than lifestyle modification alone". Orlistat was approved by Health Canada in 1999 before 2007 regulatory guidelines which defined minimal efficacy standards for medications for weight loss.⁶
- c) **Persistence:** A B.C. cohort study found that only 6% of people prescribed orlistat were still taking it at 1 year.⁷
- d) **Guidelines:** Obesity Canada's 2022 pharmacotherapy update indicates that orlistat's modest efficacy and adverse event profile limit its use.⁸ The American Gastroenterological Associations' 2022 guidelines recommend against its use.⁹

Orlistat: contraindications, adverse events, drug interactions ^{2,10,11}		
Contraindications	chronic malabsorption, cholestasis, pregnancy, lactation, pediatrics < 12 years	
Adverse events	gastrointestinal	oily spotting, flatus with discharge, increased defecation, fecal incontinence (15-50%) which are increased when taken with high fat (≥ 30%) meal; caution if pre-existing disease of the large bowel or rectum
	renal	risk of oxalate nephrolithiasis, oxalate nephropathy with renal failure; monitor renal function in patients at risk
	neuropsychiatric	headache, fatigue, anxiety
Drug interactions	oral contraceptives	switch to non-oral contraceptive or add a barrier method in cases of severe diarrhea
	vitamins	orlistat interferes with fat soluble vitamin absorption; advise patients to take a multivitamin supplement containing fat soluble vitamins (A, D, E, beta carotene); space 2 hours from orlistat or take at bedtime
	narrow therapeutic index drugs	monitor narrow therapeutic index medications for reduced effect; space cyclosporine (3 hours) and levothyroxine (4 hours) from orlistat & monitor

¹BC Provincial Academic Detailing Service 2024 Medications for weight loss in adults; ²Health Canada Drug Product Database Xenical; ³McKesson Canada Pharmaclik (accessed January 10, 2024); ⁴BC PharmaCare Formulary Search; ⁵SHI Lancet 2022;399:259-69 (PMID:34895470); ⁶US FDA 2007 Industry Guidance Weight Loss Products; ⁷PADWAL Int J Obesity 2007;31:1567-70 (PMID:17420781); ⁸Obesity Canada Pharmacotherapy Update 2022; ⁹American Gastroenterological Association Guideline Gastroenterology 2022;163:1198-25 (PMID:36273831); ¹⁰US FDA Approved Drugs Xenical; ¹¹US FDA Review Xenical 1999