

Orlistat (Xenical) over-the-counter for obesity

Summary

- Lifestyle changes involving diet, exercise and behavioural therapy are first-line for the treatment of overweight and obese patients.
- Consider pharmacotherapy when lifestyle changes alone are unsuccessful and where BMI ≥ 30 kg/m² or BMI ≥ 27 kg/m² with co-existing morbidities.
- When added to lifestyle changes, orlistat produces additional mean weight loss of 4.5 kg by reducing the absorption of dietary fat.
- Lifestyle changes should be established as early as possible with orlistat therapy to ensure successful long-term weight maintenance.
- Orlistat will not help all patients achieve the weight loss required for significant health benefits.
- Gastrointestinal adverse reactions are common with orlistat and can be controlled by modifying dietary intake of fat.
- Orlistat may reduce absorption of fat-soluble vitamins and it is recommended that supplementary doses of multivitamins be taken.

PBS listing

Although orlistat is listed on the RPBS from 1 December, this document relates to the re-scheduling of orlistat from Schedule 4 (Prescription Only) to a Schedule 3 (Pharmacist Only) medicine.

The supply of Schedule 3 medicines is made directly by a pharmacist who must provide information on its safe and effective use; refer to the Pharmaceutical Society of Australia *Standards for the Provision of Pharmacist Only and Pharmacy Medicines in Community Pharmacy* (available at <http://www.psa.org.au/media/medicines.pdf>) and *Provision of orlistat as a Pharmacist Only medicine* (available at <http://www.psa.org.au/media/orlistatprotocol.pdf>).

Reason for PBS listing

This document relates to the re-scheduling of orlistat from Schedule 4 (Prescription Only) to a Schedule 3 (Pharmacist Only) medicine.

Place in therapy

Orlistat reduces the absorption of dietary fat by inhibiting gastrointestinal lipases. Orlistat has a modest additional effect on weight loss when used in conjunction with diet, exercise and behavioural modification to treat obese patients with a body mass index (BMI) ≥ 30 kg/m² or overweight patients with a BMI ≥ 27 kg/m² and co-existing morbidities.

The National Drugs and Poisons Schedule Committee (NDPSC) agreed to re-schedule orlistat from Schedule 4 (Prescription Only) to Schedule 3 (Pharmacist Only).^{1,2} The decision was partly based on the XENDOS Study³, where orlistat had reasonable efficacy for weight reduction and lacked serious adverse effects (including vitamin deficiency and bone disease). The NDPSC also acknowledged the ability of the patient to recognise obesity and of pharmacists to provide good advice on its management and treatment, to identify co-morbid conditions and monitor for adverse effects and misuse of orlistat.^{1,2}

A possible increased risk of age-related macular degeneration (ARMD) due to impaired absorption of lutein and zeaxanthin (deficient in the retinas in ARMD) has been proposed with orlistat.² Given the lack of evidence of association between orlistat and ARMD and the low incidence of vitamin deficiencies in the XENDOS study³, this risk with orlistat is considered low.²

Monitor patients on warfarin or cyclosporin

Orlistat may reduce absorption of vitamin K and an increased International Normalised Ratio (INR) may occur with warfarin.¹³⁻¹⁵ Monitor INR when initiating or ceasing orlistat with anticoagulant therapy.¹³⁻¹⁵

Orlistat may decrease cyclosporin absorption and it is recommended to monitor plasma cyclosporin concentrations. If practical take the dose at least 2 hours before or after orlistat.¹³⁻¹⁵

Avoid orlistat in pregnancy and lactation

Orlistat should be avoided during pregnancy and lactation.¹⁴

Dosing issues

The recommended dose of orlistat is one 120 mg capsule taken during, or up to one hour after, the three main meals.^{6,13} The daily intake of fat, carbohydrate and protein should be evenly distributed, however a dose of orlistat should be omitted if a meal is missed or contains no fat.^{6,13}

Information for patients

Patients should receive the Xenical Consumer Medicine Information from either their doctor or pharmacist.

Advise patients that:

- lifestyle changes are necessary for weight loss and long-term weight maintenance.
- Orlistat has a modest additional effect on weight loss in conjunction with diet, exercise and behavioural modification and is used to achieve a weight loss of 5 to 10% of body weight that is beneficial to health.
- the diet must contain no more than 30% calories from fat (e.g. < 20 g fat per meal when the daily energy intake is 2000 calories).
- increased fat in the stools can be managed by reducing fat intake.
- it is recommended that supplementary doses of multivitamins containing fat soluble vitamins be taken 2 hours before or after a dose of orlistat or at bedtime.

For more information on obesity and lifestyle changes, refer to the Australasian Society for the Study of Obesity (ASSO) (available at <http://www.asso.org.au>), the National Heart Foundation of Australia (available at <http://www.heartfoundation.com.au>) and Nutrition Australia (available at <http://www.nutritionaustralia.org>).

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Date prepared: November 2004

The information contained in this material is derived from a critical analysis of a wide range of authoritative evidence. Any treatment decisions based on this information should be made in the context of the clinical circumstances of each patient.

Lifestyle changes are first-line for weight reduction

Diet, exercise and behavioural therapy are first-line treatments for overweight and obese patients.⁴ There is no single, effective treatment for weight reduction and a multifaceted approach is the key to successful long-term weight loss.

Use the BMI [weight (kg) divided by height squared (m²)] and waist circumference to assess obesity and the risk of co-morbidities such as diabetes, dyslipidaemia and cardiovascular disease. A BMI ≥ 30 kg/m² or waist circumference > 88 cm in women and > 102 cm in men indicates a high risk for morbidity.⁴

Table 1 outlines lifestyle changes that are effective for weight reduction.

Table 1: Lifestyle changes for weight reduction⁴

Diet
<ul style="list-style-type: none"> • Reduce daily energy intake by 2000 kilojoules (~500 to 600 calories). • Restrict the amount of fat and other energy-dense foods in the diet. • Increase the intake of high-fibre, high-water content foods (e.g. fruits, vegetables). • Maintain three balanced meals daily with low-fat, low-energy snacks in between. • Limit alcohol consumption.
Exercise
<ul style="list-style-type: none"> • Start with regular moderate-intensity exercise for at least 3 to 5 hours per week (e.g. brisk walking 30 to 60 minutes a day). • Increase the intensity of exercise only when cardiovascular fitness improves. • Maintain physical activity for at least 80 minutes a day to maintain weight loss.
Behaviour
<ul style="list-style-type: none"> • Behavioural therapy aids compliance to changes in diet and exercise and includes strategies such as counselling, hypnosis and stress management.

For more detailed information on lifestyle changes for weight reduction, refer to the National Health and Medical Research Council (NHMRC) *Clinical Practice Guidelines for the Management of Overweight and Obesity in Adults* (available at <http://www.obesityguidelines.gov.au/pdf/adults.pdf>).⁴

Set realistic goals for weight loss

A realistic goal is to reduce weight by 1–4 kg/month and achieve a weight loss of 5 to 10% of baseline body weight.⁴ This can provide substantial health benefits including reduced blood pressure and lipid levels.^{4,5}

Consider pharmacotherapy when lifestyle changes alone are unsuccessful

Consider adding pharmacotherapy when lifestyle changes do not produce a significant weight reduction after adequate trial(s) (e.g. 12 weeks).⁵ Orlistat must be used in conjunction with lifestyle changes to treat patients with a BMI ≥ 30 kg/m² or BMI ≥ 27 kg/m² with co-existing morbidities.

Orlistat produces modest weight loss in addition to lifestyle changes

Orlistat is used to assist patients with achieving a weight reduction of 5 to 10% of body weight:

- Cease orlistat if this weight reduction cannot be achieved.^{6,7}
- Use orlistat short-term to gain the greatest effect on weight loss and establish lifestyle changes as early as possible for successful long-term weight maintenance.

Orlistat in addition to lifestyle changes (e.g. hypocaloric diet containing 30% of calories from fat, exercise, behavioural intervention) had a modest additional effect on weight reduction in studies of men and women aged 18–76 years with a BMI 28–47 kg/m² and risk factors for morbidity (e.g. hypertriglyceridaemia) (see Table 2).

Table 2: Effect of orlistat on weight reduction in 1-year^{4,8-10}, 2-year^{4,11,12} and 4-year³ studies

Studies of orlistat with lifestyle changes versus lifestyle changes alone (placebo)	Mean weight reduction with lifestyle changes alone (placebo)	Mean weight reduction with orlistat (additional to placebo)
1-year studies	≤ 8.6 kg	≤ 4.5 kg
2-year studies	≤ 3.8 kg	≤ 3.4 kg
4-year XENDOS study	≤ 3.0 kg	≤ 2.8 kg

Despite long-term efficacy and safety data, the greatest benefit of orlistat is seen with shorter-term use. Results from studies may have been affected by non-compliance with lifestyle changes and possible unblinding of orlistat treatment due to adverse effects. However the available evidence suggests that the effectiveness of orlistat in weight reduction and weight maintenance is largely dependent on lifestyle changes, particularly diet.^{3,4,8-12}

In studies, orlistat plus lifestyle changes improved obesity-related risk factors (such as total cholesterol^{3,8-12}, LDL-cholesterol^{3,8-12}, LDL/HDL ratio³, triglycerides³, blood pressure^{3,8,12}, fasting blood glucose^{3,8,10,11} and insulin levels^{3,8,11,12}) more than lifestyle changes alone.

This is important for those with existing risk factors who have attained a weight loss of ≥ 5 to 10% of body weight.^{4,5,10}

Orlistat does not produce significant long-term weight loss in all patients

Orlistat will not help all patients achieve the weight loss required for significant health benefits, particularly if there is non-compliance with lifestyle changes. In the XENDOS Study³, more patients lost ≥ 5 to 10% of body weight after 1 year of orlistat plus lifestyle changes than after 4 years of treatment (see Table 3).

Studies have shown orlistat as effective for prevention of weight regain compared with placebo^{3,8-12} however weight regain may occur when a normal energy diet is resumed whilst taking orlistat or when orlistat is ceased.

Safety issues

For more information, refer to the Xenical Product Information.

Minimise gastrointestinal adverse effects by restricting fat intake

Gastrointestinal adverse effects are common with orlistat and they reinforce to patients the need to restrict fat in the diet. To minimise adverse effects, ensure that fat intake is restricted to < 20 g per meal.⁴

Gastrointestinal adverse effects in clinical trials included faecal urgency and incontinence, oily spotting, oily evacuation, fatty/oily stool, flatus with discharge, increased defecation and abdominal pain.^{8,9,11,12} In the XENDOS Study³, at least one gastrointestinal adverse effect occurred in 91% of orlistat-treated subjects (versus 65% placebo) during the first year of treatment.

Use fat-soluble vitamin supplements to prevent deficiencies

Orlistat decreased levels of fat-soluble vitamins (vitamin A, betacarotene, vitamin D, 25-hydroxyvitamin D, vitamin E and vitamin K) in studies^{3,8,9,11,12} however they remained within the reference range.

To prevent vitamin deficiencies, it is recommended that supplementary doses of fat-soluble vitamins be taken 2 hours before or after a dose of orlistat or at bedtime.^{2,13} Multivitamin supplements used in trials contained retinyl acetate 2000 IU, betacarotene up to 11,000 IU, vitamin D₃ 5 micrograms, vitamin E 14.9 mg and vitamin K₁ 36 micrograms.¹³

Table 3: Proportion of patients with $\geq 5\%$ or 10% weight loss in the XENDOS Study³

XENDOS Study duration of treatment (years)	Proportion of patients (%) with $\geq 5\%$ weight loss		Proportion of patients (%) with $\geq 10\%$ weight loss	
	Orlistat plus lifestyle changes	Lifestyle changes alone	Orlistat plus lifestyle changes	Lifestyle changes alone
1 year	73%	45%	41%	21%
4 years	53%	37%	26%	16%