

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use XENICAL safely and effectively. See full prescribing information for XENICAL.

XENICAL (orlistat) capsules, for oral use

Initial U.S. Approval: 1999

RECENT MAJOR CHANGES

- CONTRAINDICATIONS (4)
 - Pregnancy (4) Removed 9/2026
 - Known hypersensitivity to orlistat or any of the inactive ingredients in XENICAL 9/2026
- WARNINGS AND PRECAUTIONS (5) 9/2026

INDICATIONS AND USAGE

- XENICAL is an intestinal lipase inhibitor indicated in combination with a reduced calorie diet and increased physical activity to reduce excess body weight and maintain weight reduction long term in: (1)
 - adults and pediatric patients aged 12 years and older with obesity.
 - adults with overweight in the presence of at least one weight-related comorbid condition.

DOSAGE AND ADMINISTRATION

- The recommended dosage of XENICAL is one 120 mg capsule taken orally three times a day with each main meal containing fat (during or up to 1 hour after the meal). (2)
- Take XENICAL with a nutritionally balanced, reduced-calorie diet that contains approximately 30% of calories from fat. (2)
- Distribute the daily intake of fat, carbohydrate, and protein over three main meals. (2)
- Skip the dose of XENICAL if a meal is missed or contains no fat. Resume XENICAL at the next scheduled main meal containing fat. (2)
- Administer a multivitamin containing fat-soluble vitamins once daily at least 2 hours before or 2 hours after administration of XENICAL, or at bedtime. (2)

DOSAGE FORMS AND STRENGTHS

- Capsules: 120 mg.

CONTRAINDICATIONS

- Chronic malabsorption syndrome (4)
- Cholestasis (4)
- Known hypersensitivity to orlistat or any of the inactive ingredients in XENICAL (4)

WARNINGS AND PRECAUTIONS

- Loss of Effect of Certain Medications and Dietary Supplements with Coadministration of XENICAL:* Serious outcomes due to the loss of effect of cyclosporine, levothyroxine, warfarin, amiodarone, antiepileptic

drugs, antiretroviral drugs, certain fat-soluble vitamins, and beta carotene have been reported with coadministration of XENICAL. (5.1)

- Liver Injury:* Severe liver injury with hepatocellular necrosis or acute hepatic failure have been reported in patients treated with XENICAL, some cases resulted in liver transplant or death. Instruct patients to report any symptoms of hepatic dysfunction, immediately discontinue if symptoms occur and obtain liver function tests. (5.2)
- Oxalate Nephrolithiasis and Oxalate Nephropathy with Renal Failure:* Monitor renal function in patients at increased risk for oxalate nephropathy. Discontinue XENICAL in patients who develop oxalate nephropathy. (5.3)
- Acute Gallbladder Disease:* Has occurred in clinical trials and in postmarketing. If suspected, gallbladder studies and appropriate clinical follow-up are indicated. (5.4)
- Gastrointestinal Events:* May increase when XENICAL is taken with a diet high in fat (>30% total daily calories from fat). Advise patients to adhere to dietary guidelines and distribute the daily intake of fat over three main meals. (5.5)

ADVERSE REACTIONS

Most common adverse reactions (≥5% and at least twice that of placebo) include oily spotting, flatus with discharge, fecal urgency, fatty/oily stool, oily evacuation, increased defecation and fecal incontinence. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact the Safety Call Center at 1-888-236-5445 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- Cyclosporine:* Avoid simultaneous coadministration with XENICAL. Administer cyclosporine 3 hours after XENICAL. Monitor for effectiveness. (7)
- Fat-soluble Vitamin Supplements and Analogues:* Administer a multivitamin supplement at least 2 hours before or 2 hours after the administration of XENICAL, or at bedtime. (7)
- Levothyroxine:* Avoid simultaneous coadministration with XENICAL. Administer levothyroxine and XENICAL at least 4 hours apart. Monitor for changes in thyroid function. (7)
- Anticoagulants including Warfarin:* Monitor for changes in coagulation parameters. (7)
- Amiodarone:* Monitor patients as clinically indicated. (7)
- Antiepileptic Drugs:* Monitor patients for changes in seizure frequency. (7)
- Antiretroviral Drugs:* Monitor HIV RNA levels frequently and discontinue XENICAL if there is an increase in HIV viral load. (7)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 9/2026

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

XENICAL is indicated in combination with a reduced calorie diet and increased physical activity to reduce excess body weight and maintain weight reduction long term in:

- adults and pediatric patients aged 12 years and older with obesity.
- adults with overweight in the presence of at least one weight-related comorbid condition.

2 DOSAGE AND ADMINISTRATION

Recommended Dosage and Administration

- The recommended dosage of XENICAL is one 120 mg capsule taken orally three times a day with each main meal containing fat (during or up to 1 hour after the meal). Dosages above 120 mg three times a day have not been shown to provide additional benefit.
 - Take XENICAL with a nutritionally balanced, reduced-calorie diet that contains approximately 30% of calories from fat [see *Warnings and Precautions (5.5)* and *Clinical Studies (14.1)*].
 - Distribute the daily intake of fat, carbohydrate, and protein over three main meals.
 - Skip the dose of XENICAL if a meal is missed or contains no fat. Resume XENICAL at the next scheduled main meal containing fat.
 - Administer a multivitamin containing fat-soluble vitamins once daily at least 2 hours before or 2 hours after administration of XENICAL, or at bedtime [see *Warnings and Precautions (5.1)* and *Drug Interactions (7)*].

3 DOSAGE FORMS AND STRENGTHS

Capsules: 120 mg, turquoise, imprinted with “XENICAL 120” in black ink.

4 CONTRAINDICATIONS

XENICAL is contraindicated in patients with:

- chronic malabsorption syndrome [see *Warnings and Precautions (5.1)*]
- cholestasis
- known hypersensitivity to orlistat or any of the inactive ingredients in XENICAL. Serious hypersensitivity reactions, including anaphylactic reactions and angioedema, have been reported with XENICAL [see *Adverse Reactions (6.2)*].

5 WARNINGS AND PRECAUTIONS

5.1 Loss of Effect of Certain Medications and Dietary Supplements with Coadministration of XENICAL

Serious outcomes due to the loss of effect of cyclosporine, levothyroxine, warfarin, amiodarone, antiepileptic drugs, antiretroviral drugs, certain fat-soluble vitamins, and beta carotene have been reported with coadministration of XENICAL. Do not coadminister XENICAL simultaneously with cyclosporine or levothyroxine [see *Drug Interactions (7)*]. Administer cyclosporine 3 hours after the administration of XENICAL. Administer levothyroxine and XENICAL at least 4 hours apart. Administer a multivitamin supplement at least 2 hours before or 2 hours after the administration of XENICAL, or at bedtime. Monitor the effectiveness of cyclosporine, levothyroxine, warfarin, amiodarone, antiepileptic drugs, antiretroviral drugs, certain fat-soluble vitamins, and beta carotene, as clinically indicated [see *Drug Interactions (7)* and *Clinical Pharmacology (12.3)*].

5.2 Liver Injury

There have been rare postmarketing reports of severe liver injury with hepatocellular necrosis or acute hepatic failure in patients treated with XENICAL, with some of these cases resulting in liver transplant or death [see *Adverse Reactions* (6.2)]. Instruct patients to report any symptoms of hepatic dysfunction (anorexia, pruritus, jaundice, dark urine, light-colored stools, or right upper quadrant pain) while taking XENICAL. When these symptoms occur, immediately discontinue XENICAL and other suspected medications and obtain liver function tests, including ALT and AST levels.

5.3 Oxalate Nephrolithiasis and Oxalate Nephropathy with Renal Failure

XENICAL may increase levels of urinary oxalate. Cases of oxalate nephrolithiasis and oxalate nephropathy with renal failure have been reported [see *Adverse Reactions* (6.2)]. Monitor renal function when prescribing XENICAL to patients at increased risk for oxalate nephropathy, including patients with renal impairment and in those with a history of hyperoxaluria or calcium oxalate nephrolithiasis. Discontinue XENICAL in patients who develop oxalate nephropathy.

5.4 Acute Gallbladder Disease

Acute events of gallbladder disease such as cholelithiasis, have been reported in clinical trials and during the postmarketing experience with XENICAL. In a 4-year clinical trial of XENICAL, cholelithiasis was reported in 2.9% (47/1649) of XENICAL-treated patients versus 1.8% (30/1655) of placebo-treated patients. If cholelithiasis is suspected, gallbladder studies and appropriate clinical follow-up are indicated.

5.5 Gastrointestinal Events

Gastrointestinal events may increase when XENICAL is taken with a diet high in fat (>30% total daily calories from fat) [see *Adverse Reactions* (6.1)]. Advise patients receiving XENICAL to adhere to dietary guidelines [see *Dosage and Administration* (2)]. The daily intake of fat should be distributed over three main meals. If XENICAL is taken with any one meal very high in fat, the possibility of gastrointestinal effects increases.

6 ADVERSE REACTIONS

The following serious adverse reactions are described below or elsewhere in the prescribing information:

- Loss of Effect of Certain Medications and Dietary Supplements with Coadministration of XENICAL [see *Warnings and Precautions* (5.1)]
- Liver Injury [see *Warnings and Precautions* (5.2)]
- Oxalate Nephrolithiasis and Oxalate Nephropathy with Renal Failure [see *Warnings and Precautions* (5.3)]
- Acute Gallbladder Disease [see *Warnings and Precautions* (5.4)]
- Gastrointestinal Events [see *Warnings and Precautions* (5.5)]

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in patients.

Most Commonly Observed Adverse Reactions during 1 Year of Treatment

XENICAL was evaluated for safety in adults with obesity or overweight with at least one comorbid condition in seven multicenter, double-blind, placebo-controlled clinical trials of 1- to 2-years duration, and in a 4-year trial. The seven trials included 1,466 patients treated with placebo, 1,913 patients treated with XENICAL 120 mg orally three times a day, and 809 patients treated with unapproved dosages of XENICAL. Age of the patients ranged from 17 to 78 years; 80% were female, 91% White, 6% Black or African American, 2% were of Hispanic or Latino ethnicity, and 1% of other races. Six of the trials enrolled patients without type 2 diabetes mellitus (Trials 1-6) and one of the trials enrolled a population of patients with type 2 diabetes mellitus (Trial 7). The 4-year trial

(Trial 8) included 3,304 patients, age range 30-58 years; 55% were female; 99% were White and 1% other races. This trial included a subset of patients with abnormal glucose at baseline [see *Clinical Studies (14.1)*].

In placebo-controlled clinical trials, 9% of patients treated with XENICAL discontinued treatment due to adverse reactions, compared with 5% of placebo-treated patients. The most common adverse reactions that led to discontinuation of XENICAL treatment were gastrointestinal in nature. Gastrointestinal symptoms, as shown in Table 1, were the most commonly observed adverse reactions associated with the use of XENICAL in the first year of seven placebo-controlled clinical trials. In general, the first occurrence of these events was within 3 months of starting therapy.

Table 1 Adverse Reactions (5% and an incidence at least twice that of placebo) in XENICAL-Treated Adults with Obesity or Overweight for Chronic Weight Management During 1 Year of Treatment

Adverse Event	Placebo % Patients (N=1,466)	XENICAL % Patients (N=1,913)
Oily Spotting ^a	1	27
Flatus with Discharge	1	24
Fecal Urgency	7	22
Fatty/Oily Stool ^a	3	20
Oily Evacuation ^a	1	12
Increased Defecation	4	11
Fecal Incontinence	1	8

^a Oily discharge may be clear or have a coloration such as orange or brown.

Table 2 lists other adverse reactions from the seven placebo-controlled clinical trials that occurred at a frequency of $\geq 3\%$ among patients treated with XENICAL and with an incidence that was greater than placebo during year 1.

Table 2 Adverse Reactions (incidence $\geq 3\%$ and greater than placebo) from Seven Placebo-Controlled Clinical Trials During 1 Year of Treatment

Adverse Event	Placebo % Patients (N=1,466)	XENICAL % Patients (N=1,913)
Influenza	36	40
Upper Respiratory Infection	33	38
Headache	28	31
Abdominal Pain/Discomfort	21	26
Back Pain	12	14
Menstrual Irregularity	8	10
Lower Respiratory Infection	7	8
Nausea	7	8
Urinary Tract Infection	7	8
Fatigue	6	7
Arthritis	5	5
Dizziness	5	5
Anxiety	3	5

Adverse Event	Placebo % Patients (N=1,466)	XENICAL % Patients (N=1,913)
Infectious Diarrhea	4	5
Rectal Pain/Discomfort	4	5
Vaginitis	4	4
Rash	4	4
Vomiting	4	4
Otitis	3	4
Sleep Disorders	3	4
Myalgia	3	4
Tooth Disorder	3	4
Gingival Disorder	3	4

Other Adverse Reactions

Low Vitamin Levels

Table 3 illustrates the percentage of adult patients on XENICAL and placebo who developed a low blood vitamin level on two or more consecutive visits in studies up to 2 years in which patients were not previously receiving vitamin supplementation.

Table 3 Incidence of Low Blood Vitamin Values on Two or More Consecutive Visits (Adult Patients with Normal Nonsupplemented Baseline Values)

	Placebo % Patients	XENICAL % Patients
Vitamin D	7	12
Beta-carotene	2	6
Vitamin E	1	6
Vitamin A	1	2

Adverse Reactions in Patients with Type 2 Diabetes Mellitus

Hypoglycemia and abdominal distension were also reported in clinical trials in patients with type 2 diabetes mellitus and overweight or obesity.

Adverse Reactions in Pediatric Patients Aged 12 Years and Older with Obesity

In clinical trials with XENICAL in pediatric patients aged 12 years and older with obesity, adverse reactions were similar to those reported in adults [see *Clinical Studies (14.2)*].

6.2 Postmarketing Experience

The following adverse reactions have been identified during postapproval use of XENICAL. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to XENICAL exposure.

- *Immune System:* Rare cases of hypersensitivity. Signs and symptoms have included pruritus, rash, urticaria, angioedema, bronchospasm and anaphylaxis. Very rare cases of bullous eruption.
- *Gastrointestinal:* Pancreatitis; lower gastrointestinal bleeding.

- **Hepatobiliary:** Hepatitis that may be serious, and hepatic failure, with some of these cases resulting in liver transplant or death [see *Warnings and Precautions (5.2)*]; cholelithiasis [see *Warnings and Precautions (5.4)*]; increases in transaminases and alkaline phosphatase.
- **Skin and Subcutaneous Tissue:** Leukocytoclastic vasculitis. Clinical signs include palpable purpura, maculopapular lesions, or bullous eruption.
- **Renal and Urinary:** Acute oxalate nephropathy and hyperoxaluria in patients with or at risk for renal disease.

7 DRUG INTERACTIONS

Table 4 describes the clinically significant drug and dietary supplement interactions with XENICAL.

Table 4 Clinically Significant Drug and Dietary Supplement Interactions with XENICAL

Cyclosporine	
<i>Clinical Impact</i>	Coadministration of XENICAL and cyclosporine reduces cyclosporine plasma levels [see <i>Clinical Pharmacology (12.3)</i>].
<i>Intervention</i>	Avoid simultaneous coadministration of XENICAL and cyclosporine. Administer cyclosporine 3 hours after the administration of XENICAL. In those patients whose cyclosporine levels are being measured, monitor more frequently [see <i>Warnings and Precautions (5.1)</i>].
Fat-soluble Vitamin Supplements and Analogues	
<i>Clinical Impact</i>	The absorption of beta-carotene supplements is reduced when concomitantly administered with XENICAL. XENICAL also inhibited absorption of a vitamin E acetate supplement. The effect of XENICAL on the absorption of supplemental vitamin D, vitamin A, and nutritionally-derived vitamin K is not known [see <i>Clinical Pharmacology (12.3)</i> and <i>Warnings and Precautions (5.1)</i>].
<i>Intervention</i>	Administer a multivitamin supplement at least 2 hours before or 2 hours after the administration of XENICAL, or at bedtime [see <i>Dosage and Administration (2)</i>].
Levothyroxine	
<i>Clinical Impact</i>	Hypothyroidism has been reported in patients treated concomitantly with XENICAL and levothyroxine postmarketing.
<i>Intervention</i>	Avoid simultaneous coadministration of XENICAL and levothyroxine. Administer levothyroxine and XENICAL at least 4 hours apart [see <i>Warnings and Precautions (5.1)</i> and <i>Clinical Pharmacology (12.3)</i>]. Monitor patients treated concomitantly with XENICAL and levothyroxine for changes in thyroid function.
Anticoagulants including Warfarin	
<i>Clinical Impact</i>	Vitamin K absorption may be decreased with XENICAL. Reports of decreased prothrombin, increased INR and unbalanced anticoagulant treatment resulting in change of hemostatic parameters have been reported in patients treated concomitantly with XENICAL and anticoagulants.
<i>Intervention</i>	Monitor patients on warfarin or other anticoagulants who are prescribed XENICAL for changes in coagulation parameters [see <i>Clinical Pharmacology (12.3)</i>].

Amiodarone	
<i>Clinical Impact</i>	Coadministration of XENICAL and amiodarone reduces exposure to amiodarone and its metabolite, desethylamiodarone [see <i>Clinical Pharmacology (12.3)</i>]. A reduced therapeutic effect of amiodarone is possible. The effect of commencing orlistat treatment in patients on stable amiodarone therapy has not been studied.
<i>Intervention</i>	Monitor patients as clinically indicated.
Antiepileptic Drugs	
<i>Clinical Impact</i>	XENICAL may decrease the effect of antiepileptic drugs. Convulsions have been reported in patients treated concomitantly with orlistat and antiepileptic drugs.
<i>Intervention</i>	Monitor patients for changes in seizure frequency.
Antiretroviral Drugs	
<i>Clinical Impact</i>	Loss of virological control has been reported in HIV-infected patients taking orlistat concomitantly with antiretroviral drugs such as atazanavir, ritonavir, tenofovir disoproxil fumarate, emtricitabine, and with the combinations lopinavir/ritonavir and emtricitabine/efavirenz/tenofovir disoproxil fumarate. The exact mechanism for this is unclear, but may include a drug-drug interaction that inhibits systemic absorption of the antiretroviral drug.
<i>Intervention</i>	HIV RNA levels should be frequently monitored in patients who take XENICAL while being treated for HIV infection. Discontinue XENICAL if there is a confirmed increase in HIV viral load.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Available data from published prospective and retrospective cohort studies over decades of use with XENICAL during pregnancy have not identified an increased risk of major birth defects, miscarriage or other adverse maternal or fetal outcomes. However, weight loss offers no benefit to a pregnant patient and may result in a small for gestational age infant. When a pregnancy is recognized, advise the pregnant patient of the risk to a fetus and discontinue XENICAL (see *Clinical Considerations*). Oral administration of orlistat to pregnant rats and rabbits during the period of organogenesis did not show any adverse embryofetal effects at doses 23 times and 47 times, respectively, the maximum recommended human dose (MRHD) based on body surface area (mg/m²) (see *Data*).

The background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

Clinical Considerations

Disease-associated maternal and/or embryo/fetal risk

Appropriate weight gain based on pre-pregnancy weight is currently recommended for all pregnant patients, including those who have overweight or obesity, because of the obligatory weight gain that occurs in maternal tissues during pregnancy.

Data

Animal Data

In embryofetal development studies in pregnant rats and rabbits administered orlistat during organogenesis, no adverse embryofetal effects were seen at doses up to 800 mg/kg/day, corresponding to 23 times and 47 times MRHD, respectively based on body surface area (mg/m²).

In a pre- and post-natal development study in pregnant rats dosed orlistat during gestation through lactation, no adverse developmental effects were observed in the offspring at doses up to 400 mg/kg/day, corresponding to 12 times MRHD, based on body surface area (mg/m²).

8.2 Lactation

Risk Summary

There are no data on the presence of XENICAL or its metabolite in either human or animal milk, the effects on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for XENICAL and any potential adverse effects on the breastfed infant from XENICAL or from the underlying maternal condition.

8.4 Pediatric Use

The safety and effectiveness of XENICAL in combination with a reduced calorie diet and increased physical activity to reduce excess body weight and maintain weight reduction long term have been established in pediatric patients aged 12 years and older with obesity. Use of XENICAL in this indication is supported by a 54-week randomized, placebo-controlled trial in 539 pediatric patients aged 12 years and older with obesity (defined as a baseline BMI that was 2 units greater than the US weighted mean for the 95th percentile based on age and sex) [see *Clinical Pharmacology (12.2)*, *Clinical Studies (14.2)*] and from trials in adult patients with obesity [see *Clinical Studies (14.1)*]. Adverse reactions with XENICAL treatment in pediatric patients aged 12 years and older were generally similar to those reported in adults [see *Adverse Reactions (6.1)*].

The safety and effectiveness of XENICAL have not been established in pediatric patients less than 12 years of age.

8.5 Geriatric Use

Clinical studies of XENICAL did not include sufficient numbers of patients aged 65 years and older to determine whether they respond differently from younger adult patients [see *Clinical Studies (14.1)*].

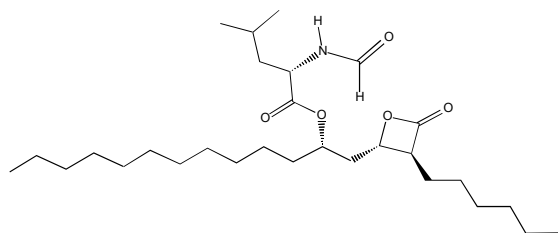
10 OVERDOSAGE

In the event of an overdose of XENICAL, consider contacting the Poison Help line (1-800-222-1222) or a medical toxicologist for additional overdosage management recommendations. Observe patients for 24 hours if an overdose of XENICAL occurs. Based on human and animal studies, systemic effects attributable to the lipase-inhibiting properties of XENICAL should be rapidly reversible.

11 DESCRIPTION

XENICAL (orlistat) is an intestinal lipase inhibitor.

Orlistat is (S)-2-formylamino-4-methyl-pentanoic acid (S)-1-[[[(2S, 3S)-3-hexyl-4-oxo-2-oxetanyl] methyl]-dodecyl ester. Its empirical formula is $C_{29}H_{53}NO_5$, and its molecular weight is 495.7. It is a single diastereomeric molecule that contains four chiral centers, with a negative optical rotation in ethanol at 529 nm. The structure is:



Orlistat is a white to off-white crystalline powder. Orlistat is practically insoluble in water, freely soluble in chloroform, and very soluble in methanol and ethanol. Orlistat has no pK_a within the physiological pH range.

Each XENICAL capsule contains a pellet formulation consisting of 120 mg of the active ingredient, orlistat, as well as the inactive ingredients microcrystalline cellulose, povidone, sodium lauryl sulfate, sodium starch glycolate, and talc. The capsule shell contains FD&C Blue No. 2 (with black printing ink containing black iron oxide, pharmaceutical grade shellac, potassium hydroxide, propylene glycol, and strong ammonium solution), gelatin, and titanium dioxide.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

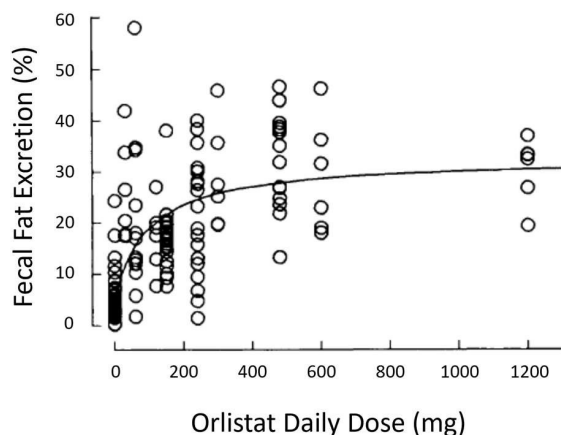
Orlistat is a reversible inhibitor of gastrointestinal lipases. It exerts its therapeutic activity in the lumen of the stomach and small intestine by forming a covalent bond with the active serine residue site of gastric and pancreatic lipases. The inactivated enzymes are thus unavailable to hydrolyze dietary fat in the form of triglycerides into absorbable free fatty acids and monoglycerides. Undigested triglycerides are not absorbed, resulting in a caloric deficit.

12.2 Pharmacodynamics

Dose-response Relationship

The dose-response relationship for orlistat in adult human volunteers is shown in Figure 1. The effect is the percentage of ingested fat excreted, referred to as fecal fat excretion percentage. Both individual data (open circles) and the curve predicted for the population with the maximum-effect model (continuous line) are shown in Figure 1.

Figure 1 Dose-Response Relationship for Orlistat in Adult Human Volunteers



At the recommended therapeutic dose of 120 mg three times a day, orlistat inhibits dietary fat absorption by approximately 30% in adult patients.

Orlistat-treated pediatric patients excreted more fecal fat daily (27% of dietary intake) than placebo-treated pediatric patients (7% of dietary intake). The magnitude of fecal fat excretion was consistent with that in adults (approximately 30%).

Ethanol does not affect orlistat's effect on preventing the absorption of fat.

Based on fecal fat measurements, the effect of orlistat is seen as soon as 24 to 48 hours after dosing. Upon discontinuation of therapy, fecal fat content usually returns to pretreatment levels within 48 to 72 hours.

Other Short-term Studies

Adult Patients

In several studies of up to 6-weeks duration, the effects of therapeutic doses of orlistat on gastrointestinal and systemic physiological processes were assessed in subjects with normal weight and with obesity. Postprandial cholecystokinin plasma concentrations were lowered after multiple doses of orlistat in two studies but not significantly different from placebo in two other experiments. There were no clinically significant changes observed in gallbladder motility, bile composition or lithogenicity, or colonic cell proliferation rate, and no clinically significant reduction of gastric emptying time or gastric acidity. In addition, no effects on plasma triglyceride levels or systemic lipases were observed with the administration of orlistat in these studies. In a 3-week study of 28 healthy male volunteers, orlistat (120 mg three times a day) did not significantly affect the balance of calcium, magnesium, phosphorus, zinc, copper, and iron.

Pediatric Patients

In a 3-week study of 32 pediatric patients aged 12 years and older with obesity, orlistat (120 mg three times a day) did not significantly affect the balance of calcium, magnesium, phosphorus, zinc, or copper. The iron balance was decreased by 64.7 $\mu\text{mole}/24$ hours and 40.4 $\mu\text{mole}/24$ hours in orlistat and placebo treatment groups, respectively. Compared to placebo, orlistat lowers BMI with greater fat mass loss than lean mass loss in pediatric patients.

12.3 Pharmacokinetics

Absorption

Systemic exposure to orlistat is minimal. Following oral dosing with 360 mg ^{14}C -orlistat, plasma radioactivity peaked at approximately 8 hours; plasma concentrations of intact orlistat were near the limits of detection

(<5 ng/mL). In therapeutic studies involving monitoring of plasma samples, detection of intact orlistat in plasma was sporadic and concentrations were low (<10 ng/mL or 0.02 µM), without evidence of accumulation, and consistent with minimal absorption.

Distribution

In vitro orlistat was >99% bound to plasma proteins (lipoproteins and albumin were major binding proteins). Orlistat minimally partitioned into erythrocytes.

Elimination

Metabolism

Based on an oral ¹⁴C-orlistat mass balance study in patients with obesity, two metabolites, M1 (the hydrolyzed β-lactone ring product of orlistat) and M3 (sequential metabolite after M1's cleavage of the N-formyl leucine side-chain), accounted for approximately 42% of total radioactivity in plasma. M1 and M3 have an open β-lactone ring and extremely weak lipase inhibitory activity (1000- and 2500-fold less than orlistat, respectively). In view of this low inhibitory activity and the low plasma levels at the therapeutic dose (average of 26 ng/mL and 108 ng/mL for M1 and M3, respectively, 2 to 4 hours after a dose), these metabolites are considered pharmacologically inconsequential. The primary metabolite M1 had a short half-life (approximately 3 hours) whereas the secondary metabolite M3 eliminated at a slower rate (half-life approximately 13.5 hours).

Plasma concentrations of orlistat and its metabolites M1 and M3 were similar in pediatric patients to those found in adults at the same dose level.

Excretion

Following a single oral dose of 360 mg ¹⁴C-orlistat in subjects with normal weight and with obesity, fecal excretion of the unabsorbed drug was found to be the major route of elimination. Orlistat and its M1 and M3 metabolites were also subject to biliary excretion. Approximately 97% of the administered radioactivity was excreted in feces; 83% of that was found to be unchanged orlistat. The cumulative renal excretion of total radioactivity was <2% of the given dose of 360 mg ¹⁴C-orlistat. The time to reach complete excretion (fecal plus urinary) was 3 to 5 days. The disposition of orlistat appeared to be similar between subjects with normal weight and subjects with obesity. Based on limited data, the half-life of the absorbed orlistat is in the range of 1 to 2 hours.

Specific Populations

No pharmacokinetic study was conducted for specific populations such as geriatric patients, patients of different races, and patients with renal or hepatic impairment.

Drug Interaction Studies

Alcohol

In a multiple-dose study in 30 normal-weight subjects, coadministration of orlistat and 40 grams of alcohol (e.g., approximately 3 glasses of wine) did not result in alteration of alcohol pharmacokinetics, orlistat pharmacodynamics (fecal fat excretion), or systemic exposure to orlistat.

Amiodarone

In a pharmacokinetic study conducted in healthy volunteers who received 120 mg orlistat three times daily for 13 days and a single dose of 120 mg orlistat on the morning of Day 14 co-administered with a single dose of 1,200 mg amiodarone on Day 4, a 23 to 27% reduction in the systemic exposure to amiodarone and desethylamiodarone was observed [see *Drug Interactions (7)*]. The effect of commencing orlistat treatment in patients on stable amiodarone therapy has not been studied.

Cyclosporine

In a multiple-dose study, coadministration of 50 mg cyclosporine twice daily with 120 mg orlistat three times daily decreased cyclosporine AUC and C_{max} by 31% and 25%, respectively. In the same study, administration of 50 mg cyclosporine twice daily three hours after the administration of 120 mg orlistat three times daily decreased cyclosporine AUC and C_{max} by 17% and 4%, respectively.

Digoxin

In 12 normal-weight subjects receiving orlistat 120 mg three times a day for 6 days, orlistat did not alter the pharmacokinetics of a single dose of digoxin.

Fat-soluble Vitamin Supplements and Analogues

A pharmacokinetic interaction study showed a 30% reduction in beta-carotene supplement absorption when concomitantly administered with orlistat. Orlistat inhibited absorption of a vitamin E acetate supplement by approximately 60%. The effect of orlistat on the absorption of supplemental vitamin D, vitamin A, and nutritionally-derived vitamin K is not known.

Glyburide

In 12 normal-weight subjects receiving orlistat 80 mg three times a day for 5 days, orlistat did not alter the pharmacokinetics or pharmacodynamics (blood glucose-lowering) of glyburide.

Nifedipine (extended-release tablets)

In 17 normal-weight subjects receiving orlistat 120 mg three times a day for 6 days, orlistat did not alter the bioavailability of nifedipine (extended-release tablets).

Oral Contraceptives

In 20 normal-weight female subjects, the treatment of orlistat 120 mg three times a day for 23 days resulted in no changes in the ovulation-suppressing action of oral contraceptives.

Phenytoin

In 12 normal-weight subjects receiving orlistat 120 mg three times a day for 7 days, orlistat did not alter the pharmacokinetics of a single 300-mg dose of phenytoin.

Pravastatin

In a 2-way crossover study of 24 normal-weight, mildly hypercholesterolemic patients receiving orlistat 120 mg three times a day for 6 days, orlistat did not affect the pharmacokinetics of pravastatin.

Warfarin

In 12 normal-weight subjects, administration of orlistat 120 mg three times a day for 16 days did not result in any change in either warfarin pharmacokinetics (both R- and S-enantiomers) or pharmacodynamics (prothrombin time and serum Factor VII). Although undercarboxylated osteocalcin, a marker of vitamin K nutritional status, was unaltered with orlistat administration, vitamin K levels tended to decline in subjects taking orlistat [see *Drug Interactions* (7)].

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

In two-year carcinogenicity studies, orlistat was given to rats and mice at doses up to 1,000 mg/kg/day and 1,500 mg/kg/day, respectively. Orlistat was not carcinogenic up to the highest doses tested in rats and mice, representing 46 times and 38 times the maximum recommended human dose, respectively, based on area under concentration vs time curve of total drug-related material.

Orlistat had no detectable mutagenic or genotoxic activity as determined by the Ames test, a mammalian forward mutation assay (V79/HPRT), an *in vitro* clastogenesis assay in peripheral human lymphocytes, an unscheduled DNA synthesis assay (UDS) in rat hepatocytes in culture, and an *in vivo* mouse micronucleus test.

No effects on fertility were observed in male and female rats given orlistat oral doses up to 400 mg/kg/day corresponding to 12 times MRHD, based on body surface area (mg/m²).

14 CLINICAL STUDIES

14.1 Weight Reduction and Long-term Maintenance Trials in Adults with Obesity or Overweight

Overview of Clinical Trials in Adults

The effects of XENICAL 120 mg administered orally three times a day on weight reduction and long-term maintenance of body weight in conjunction with a reduced calorie diet that provided approximately 30% of calories from fat were assessed in seven multicenter, double-blind, placebo-controlled clinical trials of 1- to 2-years duration, and in a 4-year trial. The seven trials included 1,466 patients treated with placebo, 1,913 patients treated with XENICAL 120 mg orally three times a day, and 809 patients treated with unapproved dosages of XENICAL. Patients were 17 to 78 years of age; 80% were female, 91% White, 6% Black or African American, 2% were of Hispanic or Latino ethnicity, and 1% were of other races. Six of the trials enrolled patients without type 2 diabetes mellitus (Trials 1-6) and one of the trials enrolled a population of patients with type 2 diabetes mellitus (Trial 7). The 4-year trial (Trial 8) included 3,304 patients; age range 30 to 58 years; 55% were female; 99% were White and 1% other races. This trial included a subset of patients with abnormal glucose at baseline.

Effect of XENICAL on Body Weight After 1 Year of Treatment

A total of 2,680 obese patients were randomly assigned to receive either placebo (n = 1,119) or XENICAL 120 mg orally three times a day (n = 1,561) for at least one year in five clinical trials. Baseline mean body weight was approximately 100 kg in the pool of Trials 1-5. A total of 1,072 (69%) patients treated with XENICAL and 701 (63%) patients treated with placebo completed 1 year of treatment. After 1 year of treatment, the mean percent weight loss difference between XENICAL-treated patients and placebo-treated patients was 3%. Greater proportions of patients treated with XENICAL achieved 5% and 10% weight loss than those treated with placebo as shown in Table 5.

Table 5 Percentage of Patients Losing ≥5% and ≥10% of Body Weight from Randomization After 1 Year of Treatment^a

Trial Number	≥5% Weight Loss					≥10% Weight Loss				
	Placebo	N	XENICAL	N	p-value	Placebo	N	XENICAL	N	p-value
1	21.3%	108	35.5%	110	0.021	6.5%	108	16.4%	110	0.022
2	27.4%	340	54.8%	343	<0.001	8.2%	340	24.8%	343	<0.001
3	26.3%	236	50.6%	241	<0.001	11.9%	236	22.8%	241	0.02
4 ^b	16.0%	212	37.1%	210	<0.001	3.8%	212	19.5%	210	<0.001
5	22.4%	223	42.6%	657	<0.001	9.9%	223	17.7%	657	0.006

^a modified intent to treat – last observation carried forward (MITT-LOCF)

^b All trials, with the exception of Trial 4, were conducted at centers specialized in treating obesity and complications of obesity. Trial 4 was conducted with primary care physicians.

Effect of XENICAL on Anthropometry and Cardiometabolic Parameters

The changes in anthropometry and cardiometabolic parameters at the end of the 1-year treatment period in the all trials population (Trials 1-5) are presented in Table 6.

Table 6 Mean Changes in Anthropometry and Cardiometabolic Parameters from Randomization Following 1 Year of Treatment^{a,b} in the All Trials Population of Clinical Trials 1 – 5

Parameter	Placebo	XENICAL
Total Cholesterol	+5.0%	-2.0%
LDL-Cholesterol	+5.0%	-4.0%
HDL-Cholesterol	+12.8%	+9.3%
Triglycerides	+2.9%	+1.34%
Systolic Blood Pressure (mmHg)	+0.58	-1.01
Diastolic Blood Pressure (mmHg)	+0.46	-1.19
Waist Circumference (cm)	-4.04	-6.45

^a modified intent to treat – last observation carried forward (MITT-LOCF)

^b Change from baseline at 1 year of treatment.

Effect of XENICAL on Body Weight After 2 Years of Treatment

The treatment effects of XENICAL were examined for 2 years in four trials (Trials 2-5). The 2-year analysis population included a total of 1,122 patients who were randomly assigned to receive either placebo (n = 516) or XENICAL (n = 606). Patients were included only if they had been randomly assigned to receive the same treatment for both years – either placebo, or XENICAL 120 mg orally three times a day– and only if they had completed the first year of treatment. At the end of year 1, the patients’ diets were reviewed and changed where necessary. The diet prescribed in the second year was designed to maintain a patient’s current weight. The mean baseline body weight was 99 kg.

The proportion of patients (pooled from four clinical trials) who completed 1 year of treatment and went on to complete a second year of therapy was 74% for XENICAL (n = 450) and 76% for placebo (n = 392). Pooled data from four clinical trials indicate that the mean weight loss difference between XENICAL 120 mg three times a day and placebo treatment groups at year 2 in those patients who completed 1 year of treatment (LOCF) was 3%. The percentages of patients achieving a $\geq 5\%$ and $\geq 10\%$ weight loss after 2 years are shown in Table 7.

Table 7 Percentage of Patients Losing $\geq 5\%$ and $\geq 10\%$ of Body Weight from Randomization After 2 Years of Treatment^a

Trial Number	$\geq 5\%$ Weight Loss					$\geq 10\%$ Weight Loss				
	Placebo	N	XENICAL	N	p-value	Placebo	N	XENICAL	N	p-value
2	23.6%	123	45.1%	133	<0.001	6.5%	123	24.8%	133	<0.001
3	27.2%	158	43.3%	178	0.002	9.5%	158	18.0%	178	0.025
4 ^b	15.0%	113	25.0%	148	0.049	3.5%	113	16.9%	148	0.001
5	27.9%	122	34.0%	147	0.279	11.5%	122	17.7%	147	0.154

^a modified intent to treat – last observation carried forward (MITT-LOCF)

^b All trials, with the exception of Trial 4, were conducted at centers specializing in treating obesity or complications of obesity. Trial 4 was conducted with primary care physicians.

The relative differences in anthropometry and cardiometabolic parameters between treatment with XENICAL and placebo were similar to the results following 1 year of therapy for total cholesterol, LDL-cholesterol, triglycerides, diastolic blood pressure, and waist circumference. The relative differences between treatment groups for HDL cholesterol and systolic blood pressure were less than that observed in the year one results.

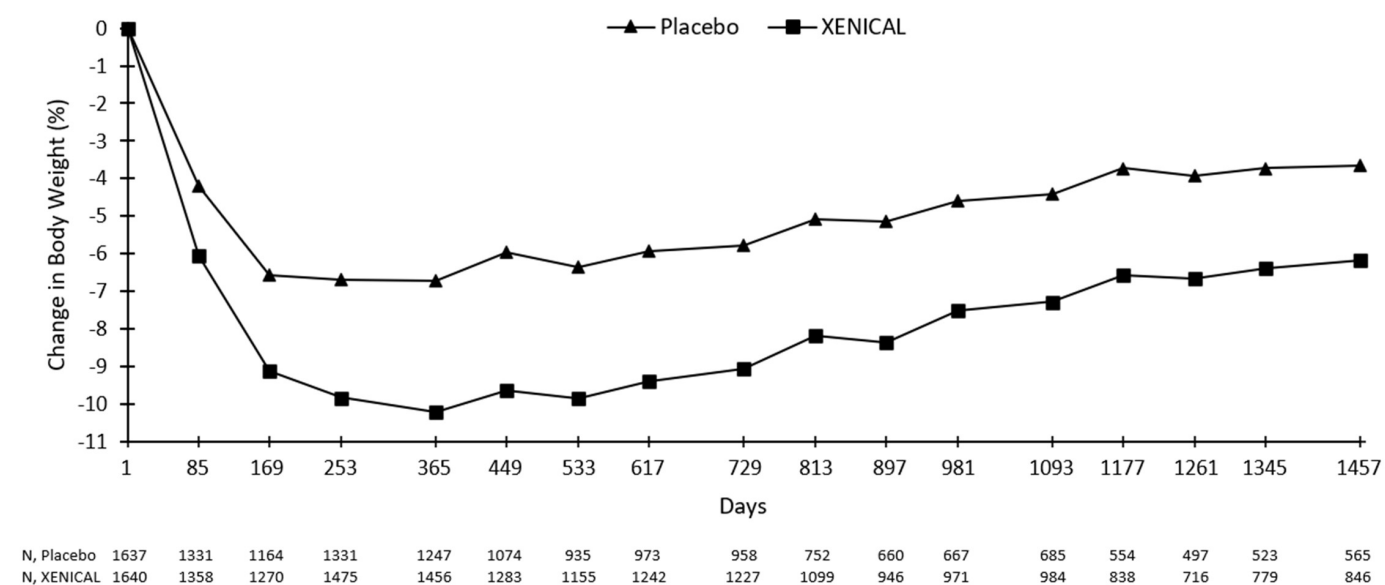
Effect of XENICAL on Body Weight After 4 Years of Treatment

In the 4-year double-blind, placebo-controlled trial (Trial 8), the effects of XENICAL on body weight were compared to placebo in 3,304 patients with obesity who had either normal or impaired blood glucose tolerance at baseline. Mean baseline body weight was 110.5 kg and mean BMI was 37.4 kg/m². A total of 564 patients (34%) of the 1,655 patients, who were randomized to the placebo group, and 850 patients (52%) of the 1,649 patients, who were randomized to the XENICAL group, completed the 4-year study.

At the end of the study, the mean percent weight loss in the placebo group was -2.75% compared with -5.17% in the XENICAL group ($p < 0.001$). Figure 2 presents mean percent change from baseline body weight observed for patients completing each study visit.

Forty-five percent of the placebo patients and 73% of the XENICAL patients lost $\geq 5\%$ of their baseline body weight, and 21% of the placebo patients and 41% of the XENICAL patients lost $\geq 10\%$ of their baseline body weight following the first year of treatment. Following 4 years of treatment, 28% of the placebo patients and 45% of the XENICAL patients lost $\geq 5\%$ of their baseline body weight and 10% of the placebo patients and 21% of the XENICAL patients lost $\geq 10\%$ of their baseline body weight. After 4 years of treatment, the mean percent difference in weight loss between XENICAL-treated patients and placebo was 2.5%.

Figure 2 Mean Change from Baseline Body Weight (%) Over Time^a



^a Observed values for patients completing each scheduled visit.

Effect of XENICAL on Body Weight in Adults with Type 2 Diabetes Mellitus and Obesity or Overweight

A 1-year double-blind, placebo-controlled trial in patients with type 2 diabetes mellitus with obesity or overweight ($n = 321$) stabilized on sulfonylureas was conducted (Trial 7). Mean baseline body weight was 99.7 kg and mean BMI was 34.3 kg/m². Following 1 year of treatment, the mean change in body weight was 6.19 kg with XENICAL and 4.31 kg with placebo ($p \leq 0.05$). Thirty percent (30%) of patients treated with XENICAL achieved at least a 5% or greater reduction in body weight from randomization compared to 13% of the placebo-treated patients ($p < 0.001$).

The changes in HbA1c and cardiometabolic parameters at the end of the 1-year treatment period in Trial 7 are presented in Table 8.

Table 8 Mean Changes in HbA1c and Cardiometabolic Parameters from Randomization Following 1 Year of Treatment^a

Parameter	Placebo	XENICAL
Total Cholesterol	+9.0	-0.9
LDL-Cholesterol	+9.5	-3.0
HDL-Cholesterol	+8.6	+6.5
Triglycerides	+16.2	+2.5
HbA1c (%)	+0.28	-0.18
Systolic Blood Pressure (mmHg)	+4.3	+0.6
Diastolic Blood Pressure (mmHg)	-0.5	-0.5

^a modified intent to treat – last observation carried forward (MITT-LOCF)

14.2 Weight Reduction and Long-term Maintenance Trial in Pediatric Patients Aged 12 Years and Older with Obesity

The effects of XENICAL on weight reduction and long-term maintenance were assessed in a 54-week multicenter, double-blind, placebo-controlled study in 539 pediatric patients aged 12 years and older with obesity (357 receiving XENICAL 120 mg three times a day, 182 receiving placebo). A similar percentage of patients in each treatment group (placebo 64%, XENICAL 65%) completed the study. The mean baseline BMI was 36 kg/m² in both treatment groups, and the mean baseline body weight was 98 kg among XENICAL-treated patients and 95 kg for placebo-treated patients. All study participants had a baseline BMI that was 2 units greater than the US weighted mean for the 95th percentile based on age and sex. The primary endpoint was percent change from baseline BMI. The mean age was 13.5 years. Most of the patients were White (XENICAL 75%, placebo 78%), Black or African American (XENICAL 19%, placebo 14%) and females (XENICAL 65%, placebo 71%).

During the study, all patients were instructed to take a multivitamin containing fat-soluble vitamins at least 2 hours before or after ingestion of XENICAL. Patients were instructed to maintain a reduced-calorie diet that provided 30% of calories from fat, 50% of calories from carbohydrate, and 20% of calories as protein. In addition, all patients were enrolled in a behavior modification program and offered counseling on physical activity.

At week 54, the least squared mean change from baseline in BMI was -0.55 kg/m² in XENICAL-treated patients and +0.31 kg/m² in placebo-treated patients (p=0.001).

The percentages of patients achieving ≥5% and ≥10% reduction in BMI and body weight after 52 weeks of treatment for the intent-to-treat population are presented in Table 9.

Table 9 Percentages of Patients with ≥5% and ≥10% Decrease in Body Mass Index and Body Weight After 1 Year of Treatment^a

	≥5% Decrease				≥10% Decrease			
	Placebo	N	XENICAL	N	Placebo	N	XENICAL	N
BMI	15.7%	178	26.5%	347	4.5%	178	13.3%	347
Body Weight	11.7%	180	19.0%	348	3.3%	180	9.5%	348

^a modified intent to treat – last observation carried forward (MITT-LOCF)

16 HOW SUPPLIED/STORAGE AND HANDLING

XENICAL is a turquoise, hard-gelatin capsule containing pellets of powder.

XENICAL 120 mg Capsules: Turquoise, two-piece, No. 1 opaque hard-gelatin capsule imprinted with XENICAL 120 in black ink — bottle of 90 (NDC 61269-460-90).

Storage and Handling

Store at 25°C (77°F); excursions permitted to 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature]. Keep bottle tightly closed.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

Loss of Effect of Certain Medications and Dietary Supplements with Coadministration of XENICAL

Advise patients taking cyclosporine, levothyroxine, warfarin, amiodarone, antiepileptic drugs, antiretroviral drugs, certain fat-soluble vitamins, and beta carotene that XENICAL may reduce their effectiveness [see *Warnings and Precautions (5.1) and Drug Interactions (7)*].

Liver Injury

Inform patients of the risk of liver injury and educate patients on the signs and symptoms of hepatic dysfunction (anorexia, pruritus, jaundice, dark urine, light-colored stools, or right upper quadrant pain). Instruct patients to contact their health care provider if they experience signs or symptoms of hepatic dysfunction [see *Warnings and Precautions (5.2)*].

Oxalate Nephrolithiasis and Oxalate Nephropathy with Renal Failure

Inform patients of the potential risk for oxalate nephrolithiasis and oxalate nephropathy and explain the associated signs and symptoms, including of renal failure. Instruct patients to contact their health care provider if they experience signs or symptoms of oxalate nephrolithiasis or oxalate nephropathy [see *Warnings and Precautions (5.3)*].

Acute Gallbladder Disease

Inform patients of the risk of acute gallbladder disease. Instruct patients to contact their health care provider for appropriate clinical follow-up if gallbladder disease is suspected [see *Warnings and Precautions (5.4)*].

Gastrointestinal Events

Inform patients of the risk of the commonly-observed gastrointestinal adverse events associated with the use of XENICAL which include oily spotting, flatus with discharge, fecal urgency, fatty/oily stool, oily evacuation, increased defecation, and fecal incontinence. Advise patients to adhere to dietary guidelines to distribute the daily intake of fat over three main meals [see *Dosage and Administration (2)*]. Advise patients that if XENICAL is taken with any one meal very high in fat, the possibility of gastrointestinal effects increases [see *Warnings and Precautions (5.5)*].

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Patient Information
XENICAL® (zen' i-cal)
(orlistat)
capsules, for oral use

Read this Patient Information before you start taking XENICAL and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment.

What is XENICAL?

XENICAL is a prescription medicine used with a reduced-calorie diet and increased physical activity to help adults and children aged 12 years and older with obesity, or some adults with excess weight (overweight) who also have weight-related medical problems to lose weight and keep the weight off. It is not known if XENICAL is safe and effective in children under 12 years old.

Do not take XENICAL if you:

- have ongoing problems absorbing nutrients from food (chronic malabsorption)
- have a bile flow problem (cholestasis)
- are allergic to orlistat or any of the ingredients in XENICAL. See the end of this leaflet for a complete list of ingredients in XENICAL

Before you take XENICAL, tell your healthcare provider about all of your medical conditions, including if you:

- have liver problems
- have kidney problems
- have problems with your thyroid
- have eating problems such as anorexia or bulimia
- have diabetes
- have a seizure disorder (epilepsy)
- have an abnormal heart rhythm (arrhythmia)
- have the human immunodeficiency virus (HIV)
- are pregnant or plan to become pregnant
- are breastfeeding or plan to breastfeed. It is not known if XENICAL passes into your breast milk.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

XENICAL and other medicines may affect each other causing side effects. XENICAL may affect the way other medicines work, and other medicines may affect the way XENICAL works. Especially tell your healthcare provider if you are taking the following medicines because they may not work as well while you take XENICAL:

- cyclosporine
- beta carotene or
- fat soluble vitamins (A, D, E, K)
- levothyroxine
- warfarin
- amiodarone
- medicines used to treat seizures (antiepileptic). Talk to your healthcare provider right away if your seizures happen more often or get worse while you take XENICAL.
- antiretroviral medicines

Know the medicines you take. Keep a list of your medicines and show it to your healthcare provider and pharmacist when you get a new medicine.

How should I take XENICAL?

- Take XENICAL exactly as your healthcare provider tells you to take it.
- Your healthcare provider will tell you how much XENICAL to take and when to take it.
- Take XENICAL with your main meals that have fat in them or up to 1 hour after your meal.
- If you miss a meal or have a meal that does not have fat in it, you can skip your dose of XENICAL. Take your next dose of XENICAL at your next scheduled main meal that has fat in it.
- If you take cyclosporine, take XENICAL 3 hours after you take cyclosporine.
- Take a multivitamin at least 2 hours before or after you take XENICAL, or at bedtime.
- If you take levothyroxine, take XENICAL and levothyroxine at least 4 hours apart.
- Spread your daily fat, carbohydrates and protein over three main meals.
- Take XENICAL with a nutritionally balanced, low-calorie diet that has no more than about 30% of calories from fat (see **Table 1**). Taking XENICAL with any meal high in fat (more than 30% fat) may make the common side effects worse.

Table 1. Recommended Daily Grams of Fat Based on Daily Calorie Intake

IF YOUR DAILY CALORIE INTAKE IS:	THE RECOMMENDED DAILY GRAMS OF FAT (in a 30% fat diet) ARE:
1500	50
1600	53
1800	60
2000	67

If you take too much XENICAL, call your healthcare provider or Poison Help line at 1-800-222-1222 or go to the nearest hospital emergency room right away.

What are the possible side effects of XENICAL?**XENICAL may cause serious side effects, including:**

- lowered absorption of certain vitamins and medicines in your body. See How should I take XENICAL?
- severe liver problems. Stop taking XENICAL and call your healthcare provider right away if you have the following symptoms of liver problems:
 - loss of appetite
 - itchy skin
 - yellowing of your skin or the white part of your eyes
 - amber-colored urine
 - light-colored bowel movements (stools)
 - pain in the upper right portion of your stomach
- kidney problems. Your healthcare provider may do certain tests to check your kidney function during treatment with XENICAL. Call your healthcare provider right away if you have the following symptoms of kidney problems:
 - swelling, especially of the legs and feet
 - little or no urine output
 - frequent or painful urination
 - blood in the urine
 - loss of appetite, nausea and vomiting
 - severe pain in the back, belly or groin
- gallbladder problems (gallstones). Call your healthcare provider right away if you have the following symptoms of gallstones:
 - pain in the upper right portion of your stomach
 - nausea
 - vomiting
- stomach problems. If you take XENICAL with a meal that is too high in fat it may increase your chance of having stomach problems. If you take XENICAL with any one meal that is very high in fat the chances that you will have stomach problems will increase. See the most common side effects

of XENICAL. Follow the diet guidelines in the How should I take XENICAL section of this patient information leaflet.

The most common side effects of XENICAL include:

- oily rectal discharge that may be clear or have an orange or brown color
- passing gas with oily discharge that may be clear or have an orange or brown color
- urgent need to have a bowel movement
- oily or fatty stools
- increased number of bowel movements
- being unable to control your bowel movements

These are not all the possible side effects of XENICAL. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store XENICAL?

- Store XENICAL at room temperature between 68°F to 77°F (20°C to 25°C).
- Keep XENICAL in a tightly closed container.

Keep XENICAL and all medicines out of the reach of children.

General information about the safe and effective use of XENICAL

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use XENICAL for a condition for which it was not prescribed. Do not give XENICAL to other people, even if they have the same symptoms that you have. It may harm them.

You can ask your pharmacist or healthcare provider for information about XENICAL that is written for health professionals.

For more information, call the Safety Call Center at 1-888-236-5445.

What are the ingredients in XENICAL?

Active Ingredient: orlistat

Inactive Ingredients: microcrystalline cellulose, povidone, sodium lauryl sulfate, sodium starch glycolate, and talc. Turquoise capsule shell: FD&C Blue No. 2 (with black printing ink containing black iron oxide, pharmaceutical grade shellac, potassium hydroxide, propylene glycol, and strong ammonium solution), gelatin, and titanium dioxide.

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