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LUBIPROSTONE (AMITIZA®): THE FIRST CHLORIDE CHANNEL ACTIVATOR FOR THE TREATMENT OF CHRONIC IDIOPATHIC CONSTIPATION

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Constipation is an exceedingly common complaint. Recent reports estimate that between 2% and 27% of North Americans suffer from constipation.[1] For many patients, constipation is a chronic condition that lasts for months and can potentially become severe. In 2002, 398,000 people were hospitalized for constipation and of these 121 deaths occurred.[2] There are many prescription and non-prescription products that have been marketed for constipation. These include the bulk-forming, osmotic, stimulant, and lubricant laxatives and stool softeners. Some patients can achieve full relief from these products, although some remain symptomatic.

The discovery of a new type of chloride channel may be the answer for those patients who have chronic constipation. Most of the chloride transport in the intestinal epithelium is through the cystic fibrosis transmembrane conductance regulator (CFTR), but it was found that there are also type 2 chloride channels (ClC-2) in these cells.[3] Lubiprostone (Amitiza® [ă mə tē′ zə]) is a new drug that activates ClC-2 channels in order to alleviate constipation. The manufacturer, Takeda Pharmaceuticals, received approval by the FDA in January 2006 to market lubiprostone for the indication of chronic idiopathic constipation in adults.[4] This article will review lubiprostone's kinetics, safety, and efficacy data.

Pharmacology and Pharmacokinetics

Lubiprostone, also referred to as SPI-0211 or RU-0211, is the first of a new class of drugs called prostones. These prostones are bicyclic fatty acids that are derivatives of a metabolite of prostaglandin E_1, though they have a negligible effect on prostaglandins E and F.[5] Type 2 chloride channels are located on the apical portion of gastrointestinal (GI) epithelium. Once they are activated, chloride moves out of these cells into the lumen of the intestinal tract. Sodium follows chloride out of the cell in order to retain neutrality. Once sodium leaves, water does as well so that isotonicity is maintained.[6] This leads to an increase in intestinal fluid so that stools are softened and motility increased. Serum electrolyte concentrations remain unaltered.[7] Lubiprostone is highly specific for ClC-2 channels; CFTR is not activated by this compound.[8]

Lubiprostone is administered orally, but due to low systemic availability, plasma concentrations are so low they cannot be quantified. Metabolism occurs by oxidation and reduction via carbonyl re-

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ductase.[7] The hepatic CYP450 system is not responsible for its metabolism, so there is a low likelihood of drug-drug interactions. Lubiprostone does not inhibit cytochrome P450 isoforms 3A4, 2D6, 1A2, 2A6, 2B6, 2C9, 2C19, or 2E1, and in-vitro studies of human hepatocytes show no induction of the cytochrome P450 isoforms 1A2, 2B6, 2C9, and 3A4. There is one active metabolite, M3, which has a C_{max} of 41.9 pg/mL and reaches peak plasma concentration after 1.14 hours. After a single oral dose of 72 mcg radiolabeled lubiprostone, 60% of the total dose was recovered in the urine within 24 hours and 30% of the was recovered in the feces by 168 hours. Food does not alter the kinetics of this drug, but it is recommended that it be taken with food to minimize nausea. Lubiprostone has not yet been studied in patients with hepatic or renal impairment.[4]

Clinical Trials

There have been a few studies published that look at the safety and efficacy of lubiprostone for treating constipation. One preclinical study focused on determining its effect on gastric/intestinal function and transit.[5] This was a randomized, double-blind, placebo-controlled study whose endpoints were meal volumes tolerated, postprandial symptoms, as well as gastric volumes in 30 healthy subjects. At 24 mcg twice a day (BID), lubiprostone increased small bowel and colonic transit, but delayed gastric emptying. Fasting gastric volume was also increased. There was no significant effect on postprandial gastric volume or symptoms associated with meals.

There were two Phase III clinical trials conducted using lubiprostone for chronic constipation. The first of the two was a randomized, double-blind, placebo-controlled trial using 242 patients with chronic constipation.[9] In this study, chronic constipation was defined as < 3 spontaneous bowel movements (SBM) per week plus at least 6 months with 1 or more symptoms from Rome II criteria (**Table 1**). Among the participants, 90% were females, 86% were white, and the average age was 48.6 years. There was a 2-week washout period before patients were randomized to lubiprostone 24 mcg BID or placebo for 4 weeks. The patients were then followed for 2 weeks with no drug to assess outcomes. Patients kept a diary to record bowel movements as well as symptoms experienced during the trial. There was a significant increase in the number of mean weekly SBM in the lubiprostone group: 5.1 to 5.7 compared to 2.8 to 3.5 in the placebo group ($p < 0.002$). A significant increase in the number of bowel movements on day one was also observed with 57% in the lubiprostone group and 37% in the placebo group ($p < 0.003$). Other improvements associated with lubiprostone included reduced straining and improved stool consistency.

Table 1. Symptoms described in Rome II criteria[10]

Straining in >25% of defecations
Lumpy or hard stools in >25% of defecations
Sensation of incomplete evacuation in >25% of defecations
Sensation of anorectal obstruction/blockade in >25% of defecations
Manual maneuvers (digital evacuation, support of pelvic floor) to help progress defecation >25% of the time
Fewer than 3 defecations/week

A second Phase III study was a double-blinded, multicenter, randomized, placebo-controlled trial of 237 patients (88% of which were females).[11] This consisted of a 15-day washout period then 28 days of lubiprostone 24 mcg BID or placebo. The primary endpoint of this study was SBM frequency. The mean weekly SBM before treatment was 1.28 in the lubiprostone group vs. 1.52 in the placebo group. After 28 days of treatment, the number of weekly SBM increased with a significant difference between groups (5.89 for lubiprostone vs. 3.99 for placebo; $p < 0.001$). There was a significant amount of patients that were classified as complete responders (defined as >4 SBM per week without using rescue drugs) in the lubiprostone group after week one compared to those who received placebo (72.1% vs. 48.7%; $p < 0.001$). In 61.3% of patients receiving lubiprostone, there was a SBM within 24 hours of the first dose, compared to 31.4% in the placebo group. **Table 2** summarizes the results of Phase III trials.

Dosing and Administration

Lubiprostone is currently available in 24 mcg gelatin capsules to be given orally. It is dosed at 24 mcg BID in adults and elderly and can be reduced to once daily if nausea is persistent. The recommended maximum dose is 48 mcg/day. It has not been studied in children and should not be recommended in this population. Lubiprostone can be taken with or

Table 2. Comparison of lubiprostone phase III trials

Study group	Design	Dose	Average SBM per week*	SBM within first 24 hrs*
Johanson et al.[9] 2003	Randomized, DB, PC N = 242	Placebo	3.1	37%
		Lubiprostone 24 mcg BID	5.3 ($p < 0.002$)	57% ($p < 0.003$)
Johanson et al.[11] 2005	Randomized, DB, PC, multicenter N = 237	Placebo	3.99	31.4%
		Lubiprostone 24 mcg BID	5.89 ($p < 0.001$)	61.3% (no p value)

SBM = spontaneous bowel movement, DB = double-blinded, PC = placebo-controlled, N = number of patients
* Comparisons to placebo

without food, although nausea may be reduced if it is taken with meals.[7] No limitations have been placed on the length of using lubiprostone.

Toxicity and Safety

Lubiprostone is safe and tolerated fairly well by patients in clinical trials. The most common adverse effects are gastrointestinal events. Nausea was the most prevalent adverse effect, occurring in 31.1% of those treated with lubiprostone compared to 5.1% in the placebo group. With all of the clinical trials combined, over 1100 patients received 24 mcg BID of lupiprostone; 3.4% reported severe nausea and 8.7% stopped treatment due to nausea. The lowest overall incidence for nausea was seen at 24 mcg/day (17.2%) and the incidence of nausea increased with

Table 3. Percentage of adverse events in greater than 1% of patients in clinical trials[4]

Adverse Event	Lubiprostone 24 mcg BID (N=1113) %	Placebo (N=316) %
Nausea	31.1	5.1
Vomiting	4.6	0.9
Headache	13.2	6.6
Diarrhea	13.2	0.9
Abdominal distention	7.1	2.2
Abdominal pain	6.7	2.8
Flatulence	6.1	1.9
Dizziness	4.1	1.3
Peripheral edema	3.8	0.3
Arthralgia	3.1	0.3
Dyspepsia	2.9	1.3
Chest pain	1.1	0.0
Dyspnea	2.4	0.0
Fatigue	2.3	1.9

higher doses. The incidence of nausea was improved when lubiprostone was taken with food; therefore, it is recommended that it be taken with a meal. Diarrhea was another common adverse effect seen in trials. Of the constipated patients that were studied, 13.2% reported diarrhea in the lubiprostone group, compared to only 0.9% of those in the placebo group. Treatment may need to be interrupted if diarrhea occurs. Other adverse reactions that occurred in more than 1% of patients are headache, abdominal distention, abdominal pain, flatulence, dizziness, peripheral edema, arthralgia, dyspepsia, chest pain, dyspnea, and fatigue.[4] **Table 3** summarizes the adverse effects reported by patients who received lubiprostone vs. placebo.

Lubiprostone is not recommended for use during pregnancy (pregnancy category C).[4] There have not been any reproductive studies done in humans. In animal models[12] fertility, reproduction, and development were not affected except at doses 166 times the recommended human dose. The adverse effects seen at these high doses were not linked directly to lubiprostone's actions, but to weight loss that occurred while taking the drug.

Cost

The average cash price of 60 capsules of lubiprostone (Amitiza®), or one month supply for most adults, is $203.49 as determined by three community pharmacies in Gainesville, FL.

Summary

Lubiprostone is a new, safe, and effective option indicated for adults with chronic idiopathic constipation. It activates the ClC-2 channel in intestinal epithelium which increases the production of intestinal fluids. This produces softer stools with more motility which gives relief to patients with chronic constipation. There are two Phase III trials that support its efficacy. Many traditional laxatives do not have sufficient data for their use.[13] Lubiprostone is not metabolized by the CYP450 system, so there is a low likelihood of drug-drug interactions. The most common adverse effect is nausea, which improves when taken with food. Lubiprostone's efficacy has been proven against placebo, but studies are still needed that compare this to other stool softeners and laxatives that have traditionally been used for constipation.

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ALLI®: AN OVER-THE-COUNTER ORLISTAT

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Obesity has become a growing problem in the United States with the incidence increasing drastically since the 1970s for both adults and children. Roughly one third of the American population is obese.[1] An individual is classified as overweight when they reach a body mass index (BMI) of 25 to 29.9 kg/m^2 and are classified as obese when they have a BMI of greater than or equal to 30 kg/m^2. A BMI of 30 is equivalent to being approximately 30 pounds overweight.[2] People are at an increased risk for mortality if they have obesity associated risk factors such as dyslipidemia, hypertension, coronary heart disease, and type 2 diabetes.[2]

There are many treatment options for obesity, the most common of which is a low calorie diet and other lifestyle changes. Other options include pharmacotherapy as well as surgery. The National Institute of Health (NIH) recommends to initially set a more realistic goal of decreasing body weight by 10%, which can decrease the severity of obesity associated risk factors. A moderate weight loss goal of 10% is attainable and will be more easily maintained for a longer period of time. Further weight loss may be possible if the patient has achieved the 10% reduction and maintained it for at least 6 months.[2]

The use of pharmacotherapy for weight loss became prevalent in the mid 1990s with the introduction of medications such as fenfluramine and dexfenfluramine. Pharmacotherapy was first introduced due to the inability to maintain weight loss from diet and physical activity alone. For approval of weight loss medications, the FDA requires at least a 5% increase in efficacy over placebo or a significantly higher number of patients achieving a 5% reduction in weight.[3] Drugs such as dexfenfluramine, fenfluramine, sibutramine, and orlistat have been studied most often in combination with lifestyle modifications such as a low calorie diet and exercise. Unfortunately, both fenfluramine and dexfenfluramine were withdrawn from the market due to an increased risk of valvular heart disease and pulmonary hypertension.[4]

Orlistat was first introduced to the market in 1999 as a prescription only obesity medication sold as the brand name Xenical®. Orlistat was the first drug for obesity to work non-systemically as a lipase inhibitor. Xenical® is available as a 120 mg tablet that is to be taken with each meal that contains fat. In 2007, the FDA granted approval to GlaxoSmithKline to market an over-the-counter (OTC) form of orlistat sold as the brand name Alli® (ăl′ ī).[5] This article will review the safety and efficacy of the lower dose of orlistat.

Pharmacology and Pharmacokinetics

Orlistat (tetrahydrolipstatin) is a synthetic derivative of lipstatin, a natural product of *Streptomyces toxytricini*. It is a reversible lipase inhibitor that works in the stomach and small intestine by forming a covalent bond with active serine residue site of gastric and pancreatic lipases. Normally in the gut, gastric and pancreatic lipases hydrolyze dietary fat in the form of triglycerides. Triglycerides are broken down to become absorbable free fatty acids (FFA) and monoglycerides (MG). Orlistat works by inhibiting these lipases so that the triglycerides are not digested and the body is incapable of absorbing FFA and MG. Orlistat has been shown to prevent the absorption of approximately 30% of dietary fat.[5]

Orlistat is administered orally, but is minimally systemically absorbed. Increased levels of fecal fat have been seen within 24 to 48 hours. Orlistat is greater than 99% protein bound, mainly to proteins such as albumin and lipoproteins. Metabolism to inactive and weakly active metabolites occurs mostly in the gastrointestinal wall. Approximately 83% of orlistat is excreted in the feces unchanged.[6]

Clinical Trials

Three clinical trials were submitted to the Food and Drug Administration to support the safety and efficacy of orlistat 60 mg as an over-the-counter product.[7,8,9] All three studies were randomized, double-blind, placebo-controlled clinical trials and all three tested the effects of orlistat in combination with a low-energy diet.

Orlistat 120 mg vs. 60 mg in Obese Patients

Orlistat's effect on weight loss was evaluated in a double-blind, placebo-controlled study.[7] The trial had a placebo run-in period where patients were

Table 1. Body weight after a 4-week placebo lead-in (day 1) and over 2 years with orlistat or placebo[7]

	Placebo		Orlistat 60 mg TID		Orlistat 120 mg TID	
	ITT	**Completer**	**ITT**	**Completer**	**ITT**	**Completer**
	N=212	N=91	N=213	N=120	N=210	N=117
Body weight at week 4 (kg)	101.8 ± 1.0	101.0 ± 0.8	100.4 ± 1.0	100.2 ± 1.5	100.5 ± 0.98	100.6 ± 1.6
Change in body weight (kg)						
Day 1	-2.73 ± 0.15	-3.2 ± 0.20	-2.49 ± 0.14	-2.98 ± 0.19	-2.54 ± 0.15	-3.03 ± 0.25
Week 24	-4.70 ± 0.60	-5.48 ± 0.52	-6.92 ± 0.64	-7.74 ± 0.54	-8.0 ± 0.58	-9.32 ± 0.62
Week 52	-4.14 ± 0.56	-4.26 ± 0.58	-7.08 ± 0.54	-7.92 ± 0.70	-7.94 ± 0.57	-8.78 ± 0.73
Week 76	-2.93 ± 0.57	-2.59 ± 0.53	-5.78 ± 0.52	-6.44 ± 0.72	-6.22 ± 0.62	-7.02 ± 0.74
Week 104	-1.65 ± 0.62	-1.54 ± 0.58	-4.46 ± 0.60	-4.58 ± 0.68	-5.02 ± 0.73	-5.16 ± 0.78

ITT = intent-to-treat, N = number of patients

tested for compliance by having pills randomly counted. If at least 75% compliance was shown, obese patients with a BMI of 30-43 kg/m^2 were randomized to either prescription orlistat (120 mg), over the counter orlistat (60 mg) or placebo. All three groups were prescribed a reduced energy diet (5020 kJ/d in patients who weighed less than 90 kg initially and 6275 kJ/d for patients who weighed 90 kg or more initially) which was nutritionally balanced and consisted of 30% energy as fat, 50% as carbohydrates, and 20% as protein, and contained a maximum of 300 mg/d of cholesterol. After the four-week placebo lead-in period, the trial duration was 104 weeks in 17 primary care centers in the United States. After the initial 52 weeks, patients received the same treatment in combination with a weight maintenance diet with the goal of preventing further weight gain. Initially 796 patients were enrolled in the study, but this number was reduced to 635 patients after the completion of the placebo lead-in period. Statistically significant weight loss was seen in both treatment groups compared with placebo throughout the two-year study ($p<0.01$). Orlistat 120 mg showed the largest decrease in weight. **Table 1** shows the changes in body weight from baseline throughout the two-year period.

Orlistat 60 mg and 120 mg effect on weight loss and cardiovascular risk factors

In a double-blind, placebo-controlled study, the efficacy of orlistat 60 mg and orlistat 120 mg on both weight as well as other cardiovascular risk factors such as dyslipidemia, hypertension, and diabetes was evaluated.[8] Patients included in the study were men and women with a BMI of 28 to 43 kg/m^2. The study consisted of three treatment groups including orlistat 120 mg, orlistat 60 mg, and placebo. After a four-week placebo run-in period, which required 75% compliance, 729 of the original 754 patients were randomized into one of three treatment groups. All three groups were also counseled by a dietician on a low energy diet that was designed to cause a 600 kcal daily energy deficit and were asked to keep a food diary. All patients were followed by a dietician every two weeks for the first two months, monthly up to month six, and then every two months for the remainder of the study. After the four-week placebo lead in period, there was a weight reduction period of 52 weeks followed by a maintenance period of 52 weeks. The primary outcome was change in body weight over time. Secondary efficacy measures included changes in cholesterol levels, blood pressure, fasting glucose, and insulin levels. **Table 2** shows the efficacy of orlistat 60 mg and 120 mg in both the intent-to-treat (ITT) population and completer populations compared to placebo. In the ITT population, both orlistat 60 mg and 120 mg had a statistically significant greater weight loss then placebo ($p<0.001$). There was not a statistically significant decline in weight for patients treated with orlistat 60 mg when compared with placebo in the completer population.

Total cholesterol ($p < 0.001$), LDL-C ($p < 0.001$), and LDL/HDL ratio ($p < 0.002$) all declined significantly in both orlistat treatment groups as shown in **Figure 1**. A significant increase in HDL

Table 2. Mean reduction in body weight for orlistat 60 mg, orlistat 120 mg, and placebo[8]

	Year 1			Year 2		
	Placebo	**Orlistat 60 mg**	**Orlistat 120 mg**	**Placebo**	**Orlistat 60 mg**	**Orlistat 120 mg**
ITT (kg)	6.4 ± 6.7	8.5 ± 7.3*	9.4 ± 6.4*	4.3 ± 7.4	6.6 ± 8.3*	7.4 ± 7.1*
Completers (kg)	7.0 ± 6.8	9.6 ± 7.3	9.8 ± 6.3*	4.3 ± 7.5	6.8 ± 8.4¶	7.6± 7.0*

ITT = intent-to-treat, * $p < 0.005$ compared to placebo, ¶ $p = 0.012$ compared to placebo

was only achieved after year one in the orlistat 120 mg group. Fasting blood glucose and diastolic blood pressure was significantly reduced after year one in the higher dose orlistat group. Reductions in fasting insulin were not seen until the end of year two and only in the orlistat 120 mg group. Secondary outcomes were not significant in the placebo group.

Orlistat 60 mg in overweight patients

In a double-blind, placebo-controlled study, the efficacy of orlistat 60 mg on weight reduction in mild to moderately overweight patients was assessed.[9] Patients included in the study were men and women with a BMI between 25 and 28 kg/m^2. The study consisted of only two treatment groups receiving either orlistat 60 mg or placebo. The study did not include a placebo run-in period and lasted only 16 weeks. All patients were instructed on maintaining a low energy diet that provided 30% energy from fat, 50% from carbohydrates, 20% as protein, no more than 300 mg/day of cholesterol, and less than 150 g/wk of alcohol. Men were allowed 1400 kcal/d and women 1200 kcal/d if they were less than 90 kg. If they were greater than or equal to 90 kg, men were allowed 1600 kcal/d and women were allowed 1400 kcal/d. No diet counseling or dieticians were involved in the study. Twenty different primary care sites in the United States screened 498 people and then randomized 391 patients. After two weeks, patients in the orlistat group had lost significantly more weight than patients taking placebo (3.05 kg vs. 1.9 kg, $p < 0.001$). **Figure 2** shows the relative change in weight loss among the two groups.

Adverse Reactions

Because orlistat is minimally absorbed, the incidence of systemic side effects is minimal. Gastrointestinal (GI) side effects were the most com-

Figure 1. Mean % change in serum total and LDL cholesterol. Adapted from Rossner et al.[8]

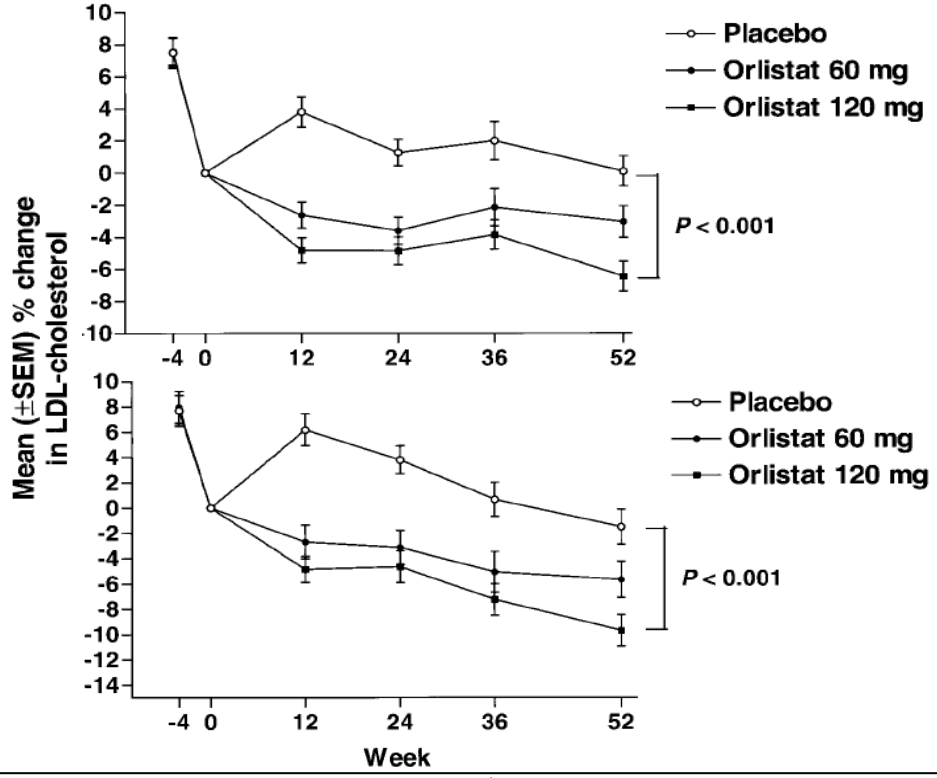
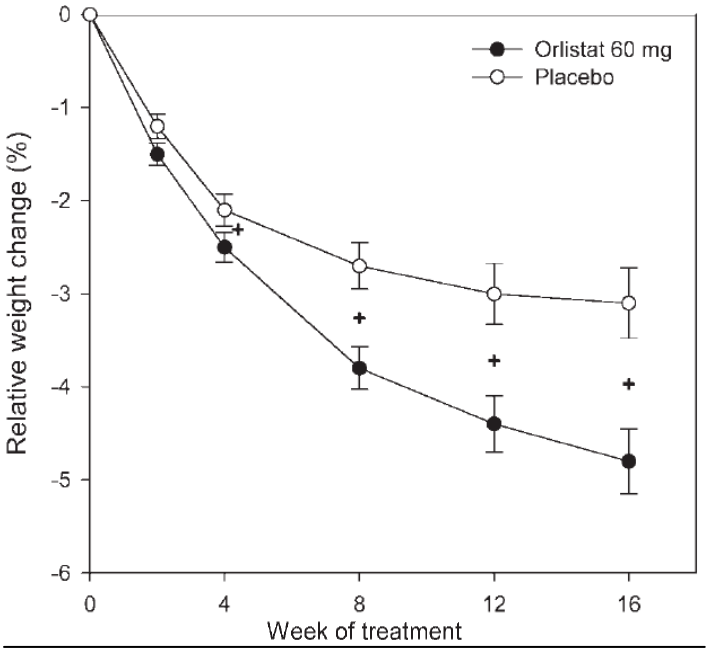


Figure 2. Relative weight change (%) for orlistat 60 mg compared to placebo. Adapted from Anderson et al.[9]



monly observed in clinical trials. **Table 3** shows the incidence of gastrointestinal events of orlistat 60 mg three times a day compared to orlistat 120 mg three times a day and placebo. Although GI events occurred in the orlistat treatment groups more frequently than the placebo group, most GI events were mild to moderate in intensity and occurred early during treatment. Most patients experienced GI events only one to two times during treatment.[7] The prescribing information states that eating a low-fat diet decreases the chances of having bowel changes.[10]

Orlistat can affect absorption of fat soluble vitamins such as vitamin A, D, and E and beta-carotene. In clinical trials, two consecutive low vitamin E and beta-carotene levels occurred more frequently in the orlistat group than in placebo. Levels of vitamin A and D did not differ between treatment groups. Upon supplementation, most patients returned to within normal range.[7] The prescribing information specifies when using OTC orlistat, vitamin supplementation should be taken at bedtime.[10]

Dosing and Administration

OTC orlistat is a 60 mg capsule which is to be taken with each fat containing meal, not to exceed 3 capsules per day. Clinical trials evaluated the efficacy of OTC orlistat only when used with a well-balanced, reduced calorie, low fat diet and regular exercise. Patients should be encouraged to exercise and follow this diet in order to optimize the efficacy of OTC orlistat as well as reduce the amount of gastrointestinal side effects.

OTC orlistat is only indicated in overweight adults who are 18 years old or older. Clinical trials evaluating the safety and efficacy of the 120 mg dose of orlistat in adolescence are underway.[11] OTC orlistat should not be used in patients with problems absorbing food, patients who are not overweight, as well as patients who have undergone an organ transplant because OTC orlistat has been shown to interact with cyclosporine.[10] Cyclosporine absorption is lipid dependent and is therefore inhibited by gastrointestinal lipase inhibitors.[5] Patients should check the height/weight chart in the label of OTC orlistat before initiating treatment to verify that they are actually overweight. The height/weight chart shown in **Figure 3** shows the weight patients should be at or above for their height before being considered overweight and eligible to take OTC orlistat.[10]

Cost

OTC orlistat is available at any community pharmacy, grocery store, or anywhere where weight loss products are sold. OTC orlistat can also be pur-

Table 3. Percentage of gastrointestinal adverse events[7]

Event*	Placebo (%)	Orlistat 60 mg TID (%)	Orlistat 120 mg TID (%)
Fecal urgency	6.6	22.5	25.2
Oily spotting	1.4	20.2	24.3
Fatty/oily stool	3.3	22.5	23.8
Flatus with discharge	2.4	25.4	18.1
Oily evacuation	0.0	12.2	11.0
Increased defecation	1.9	9.9	11.0
Fecal incontinence	0.9	6.1	6.7

*All events occurred more frequently in both orlistat treatment groups compared with placebo (P=0.001). TID = 3 times daily

Figure 3. Weight/height consideration for OTC orlistat

Ht. / Wt.	
4' 10"	129 lbs.
4' 11"	133 lbs.
5' 0"	138 lbs.
5' 1"	143 lbs.
5' 2"	147 lbs.
5' 3"	152 lbs.
5' 4"	157 lbs.
5' 5"	162 lbs.
5' 6"	167 lbs.
5' 7"	172 lbs.
5' 8"	177 lbs.
5' 9"	182 lbs.
5' 10"	188 lbs.
5' 11"	193 lbs.
6' 0"	199 lbs.
6' 1"	204 lbs.
6' 2"	210 lbs.
6' 3"	216 lbs.
6' 4"	221 lbs.
6' 5"	227 lbs.

chased online. First time users are encouraged to purchase the starter pack, which includes medication, a carrying case, and seven reference guides.[12] The starter pack comes with 90 capsules or 60 capsules which cost approximately $60.00 or $50.00.[13] After initiating OTC orlistat, the patient is encouraged to buy the refill packs which include the medication and the Read Me First Guide.[12] The Read Me First Guide includes helpful tips for patients to use in order to follow their weight loss plan. The refill pack contains 120 capsules and costs approximately $70.00.[13]

Summary

OTC orlistat is a 60 mg dose of orlistat that is now available over-the-counter. Orlistat works as a reversible lipase inhibitor which inhibits the absorption of fat. OTC orlistat is to be taken with each fatty meal up to three times daily and has been shown to be more beneficial than diet alone for both weight loss as well as reduction of other cardiovascular risk factors such as dyslipidemia. Gastrointestinal side effects may occur when taking OTC orlistat, but are reduced when the patient adheres to a low fat diet. OTC orlistat is an option for patients 18 years or older who have failed to lose weight by diet and exercise alone.

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