Efficacy, safety and tolerability of orlistat, a lipase inhibitor, in the treatment of adolescent weight excess

The treatment of childhood and adolescent obesity is difficult and the outcome of behavioral interventions remains unsatisfactory. Several pharmacological approaches, used in conjunction with comprehensive behavioral interventions designed to improve diet and decrease inactivity have been developed and extensively studied, mainly in adults. Orlistat is a lipase inhibitor that reduces dietary fat absorption by a third. It is the only pharmacological agent approved in the pediatric age group for the treatment of obesity. The goal of this article is to review the efficacy and safety of orlistat in adolescents, with emphasis on its effects on weight and body mass index, body composition and liposoluble vitamins during growth.

KEYWORDS: adolescent obesity, fat absorption, lipase inhibitor, liposoluble, vitamins, weight loss

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Adolescent obesity is one of the most refractory health problems facing the health professional today. Long-term follow-up studies indicate that obese children have a 15-fold greater risk of becoming obese adults compared with those children and adolescents who are not obese [1]. It is a chronic condition that can affect emotional and physical quality-of-life [2]. It is also the single most significant risk factor for complications such as Type 2 diabetes and cardiovascular disease. The prevalence of obesity in the pediatric age group is increasing at an alarming rate worldwide. In the USA, the proportion of obese adolescents aged 12–19 years was 15.5% in 1999–2000, compared with 10.5% in 1988–1994. This increase is even more pronounced in ethnic minorities [3]. A similar increase was observed in European countries and the prevalence of overweight adolescents is now 10–20% in northern European countries and 20–35% in southern European countries [4]. Despite constant media focus on this 'obesity epidemic', and awareness of the effects of excess body fat on health, the existing preventative and therapeutic measures have not succeeded in curbing the prevalence of adolescent obesity.

Treatment of pediatric obesity remains a difficult process. Recommended approaches classically include improved diet, decreased inactivity and long-term changes in behavior together with family involvement. However, the outcome of these interventions remains poor [5], and health professionals are turning towards adjuvant measures such as pharmacotherapy [6] and bariatric surgery [7]. Pharmacological options are presently limited in obese children and adolescents, and there is a need for new effective pharmacological agents that will promote long-term weight loss in adolescents, while offering a reassuring safety profile. Only three drugs have received extensive attention in the pediatric age group: sibutramine, metformin and orlistat. In addition, rimonabant, a specific inhibitor on cannabinoid receptor 1 that reduces food intake, is approved for the treatment of obesity in adults [8], but has to our knowledge not been investigated in adolescents. Rimonabant has not received US FDA approval and is not marketed in North America for adults or adolescents. Sibutramine is a centrally-acting serotonin–norepinephrine reuptake inhibitor that decreases appetite and was shown to cause a significant weight loss in young subjects. In a prospective, randomized, placebo-controlled, 52-week study, Berkowitz *et al.* observed that administration of 10–15 mg sibutramine in obese adolescents caused a body mass index (BMI) decrease of 2.9 kg/m^2, compared with 0.3 kg/m^2 in the placebo group [9]. All subjects took part in a comprehensive behavioral program. However, changes in blood pressure and heart rate were statistically significantly different in the sibutramine compared with the placebo group, raising the possibility of adverse long-term consequences on the cardiovascular system, and sibutramine is presently not indicated in pediatrics. Metformin is an antidiabetic agent that inhibits hepatic glucose production, increases insulin sensitivity and may decrease appetite. It is considered as a first-line approach for the treatment of Type 2 diabetes in youth. Recently, attention has focused on its potential

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as an adjuvant to behavioral weight loss interventions [10]. To date, the results are conflicting, and metformin is not presently approved for the treatment of obesity in youths [11]. Orlistat is a gastrointestinal lipase inhibitor that decreases the absorption of dietary fat. Data on the use of orlistat in adults have been reviewed in detail elsewhere [12]. The goal of this article is to provide an overview on the pediatric aspects of the efficacy, safety and tolerability of orlistat.

Competitors

Orlistat (Xenical®, Roche, Basel, Switzerland) is the only drug that acts locally in the gastrointestinal tract by inhibiting intestinal lipases and that is currently approved for the treatment of obesity in adults and adolescents. Another inhibitor of gastrointestinal lipases, cetilistat (Alizyme, Cambridge, UK), is presently under development [13]. To our knowledge, there is only one adult study published in abstract form that compares the efficacy and tolerability of orlistat and cetilistat in patients with Type 2 diabetes [14], and no data on cetilistat in adolescents.

Methods

Articles were identified using the PubMed database [101]. The keyword used was orlistat, and the search was limited to an age group of 0–18 years. All published or in press articles listed in the search until 1 September 2008 and written in English (n = 58) were screened for relevance to the topic of this review. Additional reports were identified from a review of references listed in the reports.

Pharmacological profile

Mechanism of action

Orlistat is a chemically synthesized derivative of lipstatin, a natural product of *Streptomyces toxytricini*. Its empirical formula is $C_{29}H_{53}NO_5$, and its molecular weight is 495.7. Orlistat 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. This prevents hydrolysis of the dietary triglycerides into absorbable free fatty acids and monoglycerides [15,16]. The calorie deficit caused by decreased fat absorption is thought to be the main mechanism by which orlistat causes weight loss. Therefore, systemic absorption of the drug is not needed for activity. At the recommended therapeutic dose of 120 mg three-times daily, orlistat inhibits dietary fat absorption by approximately 30% in adults [17]. Similar findings have been reported in adolescents. Zhi *et al.* investigated 32 male and female obese adolescents from Caucasian, Black or Hispanic ethnicity [18]. Compared with the placebo group, orlistat given at the dose of 120 mg three-times daily for 7 days, increased fat excretion from 4.1 (6.1%) to 15.9 g/day (27.1%).

Pharmacokinetics

The pharmacokinetics of orlistat in adults has been described in detail elsewhere [19]. More than 97% of the drug is excreted in the feces, mostly as the parent compound (83%). Systemic absorption of orlistat is minimal. In the circulation, orlistat is mostly bound to proteins (>99%) and is partially metabolized into two pharmacologically inactive metabolites, M1, which results from hydrolysis of a β-lactone ring and M3, which results from the cleavage of the N-formyl leucine side chain of M1. In obese adolescents, mean plasma concentrations of orlistat measured at weekly intervals 4 h following administration of the dose, a time corresponding to the expected peak concentration, ranged from 0.4 to 0.9 ng/ml. These values were 24 to 33 ng/ml for M1 and 45 to 117 ng/ml for M3 [18], and are similar to those observed in adults during continuous administration of orlistat at the recommended dose of 120 mg three-times daily [20].

Clinical efficacy

Orlistat has been studied extensively in adults, and was shown to be more effective than placebo in promoting weight loss, as well as in improving obesity-related risk factors in obese patients with and without metabolic complications [12,21]. By contrast, the number of studies assessing the efficacy of orlistat in children and adolescents is small. To our knowledge, no Phase I or II trials were performed in the pediatric age group. Several Phase III trials were performed in children and adolescents, although only two were randomized and placebo-controlled. All pediatric studies used a dose of orlistat that was identical to the adult recommendations (120 mg three-times daily).

Anthropometry & body composition

Chanoine *et al.* performed a 52-week randomized, double-blind, placebo-controlled trial in 539 adolescents with uncomplicated obesity (Table 1) [22]. Statistical analysis was performed on 533 patients who received at least one dose of the medication. A total of 76% of subjects

were of Caucasian origin. All patients received a mildly hypocaloric diet, behavioral modification and were given a multivitamin supplementation. There was a decrease in BMI and weight in both treatment groups, which was maximal by 12 weeks and greater in the orlistat group. After 12 weeks, BMI remained stable in the orlistat group, but increased back beyond baseline with placebo. At the end of the study, BMI had decreased by 0.55 kg/m^2 in the orlistat group, but increased by 0.31 kg/m^2 in the placebo group ($p = 0.001$). Weight had increased by 0.53 kg with orlistat and by 3.14 kg with placebo ($p < 0.001$). Waist circumference decreased in the orlistat group, but increased in the placebo group (-1.33 cm vs +0.12 cm; $p < 0.05$). Dual-energy x-ray absorptiometry demonstrated that the difference in body mass was fully explained by changes in fat mass. Overall, subjects in the orlistat group were 1.7-times more likely to experience a 5% or higher BMI decrease (26.5 vs 15.7%) and three-times more likely to experience a 10% or higher BMI decrease (13.3 vs 4.5%). The factors associated with a better response to orlistat treatment are unclear. Subanalysis of these results did not reveal ethnic- or sex-specific differences. Similar to what was observed in adults [23], an early response to orlistat was the best prognosis factor for a greater weight loss at 12 months. Those subjects who experienced a weight loss greater than 5% after 12 weeks of treatment had a mean BMI decrease of 3.7 kg/m^2 at 12 months, contrasting with an increase in 0.1 kg/m^2 in subjects who lost less than 5% of their body weight at 12 weeks [24].

Using a similar study design, Maahs *et al.* performed a 6-month randomized, double-blind, placebo-controlled trial that included 40 obese adolescents (**Table 1**) [25]. A total of 62% of the adolescents were of Hispanic origin. The intervention consisted of a calorie-restricted diet (500 kcal deficit) and a behavioral modification in both groups. All subjects received multivitamin supplementation. A statistically significant decrease in weight and BMI was observed in both the placebo and the orlistat groups. At 6 months, weight (-5.5 vs -1.6 kg) and BMI (-1.3 vs -0.8 kg/m^2) changes tended to be greater in the orlistat compared with the placebo group. The magnitude of these differences was roughly similar to those observed in the 1-year trial described previously [22], but did not reach statistical significance, likely reflecting the small number of subjects included in the trial and the variability of the individual responses in both placebo and orlistat groups.

Table 1. Summary of key aspects described in clinical studies in obese adolescents treated with orlistat.

Study	Design	Number of patients	Baseline age (years)	Drop out (%)	Duration (months)	Baseline weight (kg)	Baseline BMI (kg/m^2)	Weight change (kg)	BMI change (kg/m^2)	Ref.
Chanoine *et al.* (2005)	Randomized, double-blind	Pla: 181 (129 F/52 M) Orl: 352 (228 F/124 M)	Pla: mean 13.5 (SD: 1.2) Orl: mean 13.6 (SD: 1.3)	Pla: 36 Orl: 35	12	Pla: mean 95.1 (SD: 14.2) Orl: mean 97.7 (SD: 15.0)	Pla: mean 35.4 (SD: 4.1) Orl: mean 35.7 (SD: 4.2)	Pla: LSM +3.14 Orl: LSM +0.53 ($p < 0.001$)	Pla: LSM +0.31 Orl: LSM -0.55 ($p = 0.001$)	[22]
McDuffie *et al.* (2002, 2004)	Open-label	20 (10 F/10 M)	Mean 14.6 (SD: 2.0)	25	6	Mean 123.4 (SD: 43)	Mean 44.1 (SD: 12.4)	Mean -5.4 ($p < 0.02$)	Mean -2.0 ($p = 0.001$)	[27,28]
Maahs *et al.* (2006)	Randomized, double-blind	Pla: 20 (15 F/5 M) Orl: 20 (12 F/8 M)	Pla: mean 15.8 (SD: 1.5) Orl: mean 15.8 (SD: 1.4)	Pla: 10 Orl: 20	6	Pla: mean 114.3 (SD: 38.4) Orl: mean 111.1 (SD: 22.9)	Pla: mean 41.7 (SD: 11.7) Orl: mean 39.2 (SD: 5.3)	Pla: mean -1.6 Orl: mean -5.5 NS	Pla: mean -0.8 (SD: 3.0) Orl: mean -1.3 (SD: 1.6) NS	[25]
Norgren *et al.* (2003)	Open-label	11 (7 F/4 M)	Median 10.7 (range: 8.3–12.3)	0	3	Median 73.2 (range: 53.5–103.1)	Median 33.3 (range: 27.6–37.5)	Mean -1.7 (range: -12.7 to +2.5) ($p = 0.016$)	Mean -1.9 ($p = 0.008$)	[29]
Ozkan *et al.* (2004)	Randomized	Con: 20 (10 F/5 M in 15 completers) Orl: 22 (10 F/5 M in 15 completers)	Con: mean 12.5 (SD: 2.2) Orl: mean 12.9 (SD: 2.4)	Pla: 32 Orl: 25	Con: mean 10.2 (SD: 3.7) Orl: mean 11.7 (SD: 3.7)*	Con: mean 73.9 (SD: 15.3) Orl: mean 82.1 (SD: 20.9)	Con: median 31.2 Orl: median 32.5	Con: mean + 4.16 (SD: 6.45)* Orl: mean -6.27 (SD: 5.4)* ($p < 0.001$)	Con: + 0.11 (SD: 2.49)* Orl: -4.09 (SD: 2.9)* ($p < 0.001$)	[26]

Duration of the trial and outcome measures are provided only for the 15 subjects who completed the study. p-values reflect the significance of the differences between baseline and end of the study (open-label studies) or between the changes in each group (randomized studies).
Con: Control group; F: Female; LSM: Least squares mean; M: Male; NS: Not significant; Orl: Orlistat group; Pla: Placebo group; SD: Standard deviation.

Ozkan *et al.* followed two groups of obese adolescents for almost a year (TABLE 1) [26]. All patients received multivitamins, were given a mildly hypocaloric diet (20% reduction in daily calories) and were advised to perform at least 30 min of exercise per day. Subjects in the control group did not receive placebo. The subjects receiving orlistat lost 6.3 kg compared with a gain of 4.2 kg in the control group ($p < 0.001$). However, these results only include data from the subjects who completed the study (15/22 in the orlistat group and 15/20 in the placebo group).

Two smaller open-label studies were also performed in adolescents. McDuffie *et al.* investigated 20 obese adolescents from African–American (n = 10) and Caucasian (n = 10) origin for up to 6 months (TABLE 1) [27,28]. In contrast with the above studies, all subjects had at least one obesity-related comorbid condition. All subjects participated in a behavioral program aiming at increasing physical activity and improving nutrition, and were given a 500-kcal-deficient diet and received daily multivitamins. Overall, weight decreased by 5.4 kg (range: +11.7 to -25.5 kg). Interestingly, orlistat did not significantly affect body mass or -composition in African–American subjects, and changes in weight (-7.86 vs +0.36 kg; $p < 0.05$), BMI Z-score (-1.10 vs + 0.29; $p < 0.03$) and waist circumference (-8.65 vs -1.59 cm; $p = 0.03$) were significantly greater in Caucasian compared with African–American adolescents. Whether these different responses are related to the ethnic background is unclear. African–American adolescents were markedly heavier than Caucasian subjects at baseline (136.7 vs 99.3 kg), had lower resting energy expenditure at baseline and experienced a greater resting energy expenditure decrease than Caucasian subjects during treatment. Finally, Norgren *et al.* followed 11 obese prepubertal children of Caucasian origin for 3 months [29]. Dietary information was provided at inclusion. Orlistat was associated with a median weight loss of 4 kg ($p = 0.016$). Mean body fat decreased by 3% ($p = 0.008$).

Biochemical data

Markers of glucose homeostasis as well as lipid profile were reported in all [22,25,27–29] but one study [26]. In one open-label study [27], where subjects had at least one obesity-related condition, orlistat was associated with statistically significant decreases in total cholesterol (-13%), low-density-lipoprotein cholesterol (-17%) and fasting insulin (-27%) ($p \leq 0.002$) after 6 months. In three other studies, fasting glucose, insulin, triglycerides and cholesterol were unaffected by orlistat treatment [22,25,29]. However, in these studies, markers of metabolic complications were largely within the normal range at baseline, suggesting that these subjects had mostly uncomplicated obesity.

Safety

Orlistat is minimally absorbed, and no safety issues relative to its systemic action have been raised. The safety of orlistat has been observed for up to 4 years in adults [30], and up to 1 year in adolescents [22]. A potential consequence of the decreased absorption of dietary fat caused by orlistat, is a decrease in the absorption of fat-soluble vitamins. McDuffie *et al.* compared plasma vitamin concentrations following acute administration of vitamin A (100,000 U retinol palmitate) or vitamin E (20 UI/kg α-tocopherol) in 17 obese adolescents before and during orlistat treatment [31]. Vitamin A absorption was unaffected by orlistat but there was a decrease in the peak of α-tocopherol concentrations with orlistat. The chronic effects of orlistat (administered in conjunction with multivitamin supplementation) on plasma vitamin concentrations were also measured in the same study. The plasma concentrations of retinol, cholecalciferol (except for a transient 22% decrease after 4 weeks of treatment), α-tocopherol and phylloquinone were not affected by orlistat for up to 24 weeks. In a 52-week prospective study in obese adolescents where all subjects received a multivitamin supplementation, we observed similar concentrations of vitamins A, D and E, as well as retinol, in placebo- and orlistat-treated study groups [22]. Maahs *et al.* found no difference in vitamin A, D and E concentrations between the placebo and the orlistat groups followed for 6 months and receiving multivitamin supplementation [25]. In an open-label study, only a transient decrease in vitamin A and E was observed in 11 subjects receiving orlistat for 12 weeks [29]. These data are similar to those reported in adult studies [30,32,33].

Since puberty is a period of positive energy balance, the effect of orlistat on mineral, electrolytes and body composition has been specifically studied in adolescents. Zhi *et al.* investigated the effect of orlistat administration on calcium, copper, iron, magnesium, phosphorus and zinc in two groups of obese adolescents receiving placebo or orlistat for 21 days, and found no effect of orlistat on the balance of these minerals [18]. Similar to adults, a modest decrease in iron balance was observed in adolescents during

the study in both placebo and orlistat groups [33]. Similarly, sodium and potassium serum and urine concentrations were not affected by orlistat. In a 52-week randomized study, no difference in the progression of puberty and in the increase in lean mass associated with pubertal growth was observed between the placebo and orlistat groups [34]. Taken together, these data suggest that orlistat does not affect the anabolism of puberty for at least 1 year.

The potential effects of orlistat on the absorption of other drugs have been mainly studied in adults and have been reviewed in detail elsewhere [12]. Generally, orlistat has little effect on the absorption of oral medications. However, several reports have demonstrated a decrease in the absorption of amiodarone (-25%) [35] and cyclosporine (-30%) [36] in adult volunteers receiving orlistat. This has, to our knowledge, not been reported in pediatric patients.

Orlistat was associated with an increase in the frequency of seizures in an 18-year-old subject with known epilepsy, raising the possibility that absorption of lamotrigine, an antiepileptic medication thought to be lipophilic, was decreased [37]. Another case report potentially linking orlistat to worsening of diabetes has been reported in an 18-year-old subject. This young adult with known Type 1 diabetes developed diabetes ketoacidosis despite an increase in the insulin dose one month after starting orlistat. Dehydration secondary to watery stools was thought to be the mechanism behind this complication [38].

The effect of orlistat in patients with bulimia nervosa has been investigated in adults. In this setting, orlistat causes a greater weight loss compared with placebo after 24 weeks of treatment [39] but does not affect the eating behavior [40]. Importantly, orlistat was also shown to be used for purging following binge episodes in two young women diagnosed with bulimia nervosa during adolescence [41]. Considering the high prevalence of eating disorders in obese adolescents [42], the health practitioner should be aware of this potential misuse of orlistat in adolescents with bulimia nervosa.

Finally, the effects of accidental ingestion of orlistat was described in 106 patients aged 5 years or less (mean dose 155 mg; range: 30–600 mg) and was associated with no or minor side effects [43].

Tolerability

Consistent with the inhibition of intestinal lipases, orlistat causes an increase in fecal fat excretion. As a consequence, gastrointestinal side effects that are generally mild-to-moderate in intensity have occurred in subjects receiving orlistat. The pattern of these effects has been discussed in-depth in adults [12]. In a prospective, 52-week study, the most common side effects were fatty or oily stools (50% of the subjects receiving orlistat vs 8% in the placebo group), oily spotting (29 vs 4%), oily evacuation (23 vs 2%), abdominal pain (22 vs 11%), fecal urgency (21 vs 11%), flatus with discharge (20 vs 3%), soft stools (15 vs 11%) and flatulence (9 vs 4%). These side effects were transient in a majority of the subjects, and only 16% of the subjects experienced fatty or oily stools, the most common side-effect, more than once [22]. The reason for this decrease with time is unclear, but could be linked to behavioral changes aiming at decreasing the fat content of the diet in order to prevent their occurrence. This assumption is supported by the association between olestra intake and worsening of gastrointestinal side-effects with orlistat in a 16-year-old African–American obese girl [44]. The subject started orlistat as part of a comprehensive weight loss intervention and experienced severe gastrointestinal side-effects. She was inadvertently consuming high quantities of olestra, a fat substitute that contains 6–8 fatty acid chains arranged around a molecule of sucrose from which they cannot be separated. Removal of olestra from the diet markedly decreased the gastrointestinal side effects associated with orlistat. These data suggest that adherence to a low-fat diet while using orlistat helps prevent the gastrointestinal side effects. In adults, the concomitant use of natural fibers, such as psyllium husk in the diet was shown to prevent the gastrointestinal side effects [45].

It is important to note that the tolerability of orlistat has been mostly evaluated in carefully designed clinical trials where extensive information was provided to the subjects. In day-to-day clinical practice, health practitioners should make every effort to ensure that the mechanisms of action, as well as the potential side effects of orlistat, are explained to the patient. The importance of adhering to an appropriate diet should also be emphasized.

Other pediatric use

The increase in fecal fat excretion caused by orlistat has been exploited to decrease the enterohepatic cycle of unconjugated bilirubin and, as a consequence, decrease the plasma concentrations of unconjugated bilirubin in patients with Crigler Najar disease. In seven out of 16 patients (median age 17.7 years; range:

8–51 years) with this genetic disorder, caused by deficiency of the hepatic enzyme bilirubin–uridine diphosphate–glucuronosyltransferase and characterized by chronic unconjugated hyperbilirubinemia, orlistat caused a decrease in unconjugated hyperbilirubinemia greater than 10% that was positively correlated with fecal fat excretion [46]. These preliminary data suggest that orlistat may be useful in selected patients with this rare condition.

Regulatory affairs

The recommended dose of orlistat (Xenical®, Roche) is 120 mg three-times daily for both adults and adolescents. It is indicated for obese adults with a BMI of 30 kg/m^2 or more, or 27 kg/m^2 or more in the presence of other risk factors. These values correspond roughly to the 95th and 85th percentiles for BMI on the Center for Disease Control growth charts [102]. In the USA, orlistat is also marketed for obese adults as an over-the-counter medication at the dose of 60 mg three-times daily with meals containing fat (Alli®, GlaxoSmithKline, London, UK).

Orlistat received approval from the FDA in December 2003 for the treatment of obesity in adolescents aged 12–17 years in the USA. In Europe, orlistat received a positive opinion from the Committee for Medicinal Products for Human Use in May 2005 to include data on its use in obese adolescents aged 12 years and over. In addition, orlistat is approved with a prescription for use in obese adolescents 12 years and older in Bahrain, China, Cuba, Hong Kong, Mexico, Singapore, Switzerland, Taiwan and Vietnam. It is also available as an over-the-counter medication, at the dose of 120 mg three-times daily, in obese adolescents 12 years (Philippines and Thailand) or 13 years (Malaysia) and older.

Conclusion

We have reviewed the efficacy, safety and tolerance of orlistat, a gastrointestinal lipase inhibitor, in the treatment of obesity in children and adolescents. Orlistat is the first and only pharmacological agent approved in adolescents aged 12 years and above. At the dose of 120 mg three-times daily (one tablet of 120 mg with each main meal), it promotes additional weight loss compared with placebo, when administered in association with a comprehensive approach that includes dietary modification, decreased inactivity and long-term modifications in behavior and lifestyle. Similar to adults, there is a large individual variability in the results obtained with orlistat and it is presently difficult to reliably predict the response to orlistat treatment in individual patients. However, preliminary results suggest that a loss of more than 5% body weight after 12 weeks of treatment identifies the subjects who achieve a clinically significant weight loss at 52 weeks. Whether orlistat should be proposed at the initiation of a comprehensive intervention or after failure of this intervention has not been investigated in adolescents. The side effects of orlistat are limited to the gastrointestinal sphere and are generally mild and limited in duration.

The authors suggest the following practical approach:

- Orlistat can be proposed to obese adolescents older than 12 years, at the dose of 120 mg three-times daily, in conjunction with a comprehensive behavioral intervention;
- The importance of adhering to a proper diet as well as the side effects associated with orlistat should be discussed with the adolescent (and the family as appropriate) prior to the start of the treatment;
- The decision to pursue orlistat treatment should be reevaluated after 12 weeks on basis of the initial weight loss achieved by the subject;
- Multivitamin supplementation should be prescribed with orlistat;
- Obesity is a chronic condition and long-term intervention is expected. It should, however, be kept in mind that efficacy and safety data are available with orlistat for up to 4 years in adults, but only up to 1 year in adolescents.

Executive summary

- Orlistat inhibits the activity of intestinal lipases and decreases dietary fat absorption by a third.
- It is the only pharmacological agent approved for the treatment of obesity in adolescents aged 12 years and above.
- Compared with placebo, orlistat, in conjunction with a comprehensive behavioral approach, causes on average an additional body mass index (BMI) decrease of 0.86 kg/m^2 after 12 months of treatment.
- A weight loss greater than 5% after 12 weeks of treatment with orlistat predicts a BMI decrease of 3.7 kg/m^2 after 12 months of treatment.
- Orlistat does not affect pubertal development or the increase in lean body mass during puberty.
- Gastrointestinal side effects, such as fatty and oily stools, are consistent with its mechanism of action and tend to be moderate and transient.
- Multivitamin supplementation is advised during orlistat treatment to prevent the potential decrease in liposoluble vitamin concentrations.

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